

Systematic review of pharmacogenomics in psoriasis

AC Foulkes,¹ A Jorgensen,² M Pirmohamed,² CE Griffiths¹ and RB Warren¹ ¹ The Dermatology Centre, University of Manchester, Manchester, United Kingdom and ² Wolfson Centre for Personalised Medicine, Liverpool, United Kingdom

Pharmacogenetic and pharmacogenomic studies have investigated biomarkers of drug efficacy and toxicity in psoriasis, yet none have translated into clinical care. We performed a systematic review of publications assessing the influence of genetic/genomic variation on treatment response in psoriasis patients. Studies were included where: participants had a diagnosis of psoriasis; a genomic test was performed; response to treatment was documented with a defined outcome measure and treatment response was correlated with the genomic test. Four electronic databases were searched from inception to August 2012. In total 27,203 abstracts were scanned, from which 121 full papers were evaluated; only 45 studies, published between 1995 and 2012, met inclusion criteria. Therapies evaluated included 9 topical, 8 phototherapy, 8 systemic, 19 biologic and 3 novel immunotherapies. Of the 26 pharmacogenetic and 19 pharmacogenomic studies, only 2 reported undertaking a sample size calculation before patient recruitment. A positive association with efficacy or toxicity and genetics/genomics was reported by 33 studies. Sources of heterogeneity included: poor phenotyping of participants; failure to define treatment response using validated methodology; timing of measurement of response and; documentation of participants' concurrent therapies. Key quality control data were rare, including accuracy of genotyping in pharmacogenetic studies (2 of 26) and derivation of statistically significant fold change in gene expression. To realise the power of genomics in the field of personalised medicine, genomic screening prior to psoriasis therapy must be accurate and effective in predicting response and in preventing adverse reactions. Thus we recommend: high quality phenotyping of participants; publication of reproducible methodology including a priori power to detect association; use of a validated outcome measure for measurement of psoriasis and; a clear definition of response.

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Association between the type and length of tumor necrosis factor (TNF) inhibitor therapy and myocardial infarction (MI) risk in psoriasis

JL Wu,¹ KT Poon² and JD Bechuk² ¹ Dermatology, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA and ² Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA

We sought to assess whether the type of TNF inhibitor therapy (soluble receptor versus monoclonal antibody) has an effect on the association of MI risk, and determine whether length of TNF inhibitor therapy has an effect on the association of MI risk. This was a retrospective cohort study from January 1, 2004 and November 30, 2010 of at least 3 ICD9 codes for psoriasis (696.1) or psoriatic arthritis (696.0) without antecedent MI. In the 3 subgroups of TNF inhibitors, 976 received etanercept only; 217 received monoclonal antibody only; and 480 received etanercept or monoclonal antibody. In the Cox proportional hazards analysis, etanercept only (HR, 0.53; 95% CI, 0.31-0.92) was associated with a significant reduction of MI risk compared to topical agents, and monoclonal antibody only (HR, 0.25; 95% CI, 0.06-1.03) and etanercept or monoclonal antibody (HR, 0.53; 95% CI, 0.27-1.06) were associated with a non-significant reduction of MI risk compared to topical agents. Using year 1 as reference, those who received TNF inhibitor therapy at year 2 (HR, 0.71; 95% CI, 0.19-2.67) had a non-significant reduction of MI risk; and those who received TNF inhibitor therapy at year 3 (HR, 1.51; 95% CI, 0.52-4.35) and at year 4 (HR, 1.25; 95% CI, 0.50-3.11) had a non-significant increase of MI risk. Treatment with etanercept compared to treatment with topical agents, was associated with a significant decreased risk of MI in psoriasis patients. Treatment with monoclonal antibody only and etanercept or monoclonal antibody, compared to treatment with topical agents, was associated with a non-significant decreased risk of MI risk in psoriasis patients. There was a trend that those treated with TNF inhibitors at year 3 or 4 had a non-significant increased risk of MI compared to those who were treated with TNF inhibitors at year 1.

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Thanakha and its dermatologic uses in Myanmar (Burma)

EV Seiverling¹ and HT Ahn² ¹ Dermatology, The Vancouver Clinic, Vancouver, WA and ² Family Medicine, Oregon Health and Science University, Portland, OR

Recent geopolitical changes in Myanmar have resulted in new opportunities to study skin health and disease in a previously isolated population. This cross-sectional study investigated the dermatologic uses of thanakha in Myanmar. Used by Burmese people for over 2,000 years, thanakha powder is produced by grinding the bark of *Hesperethusa crenulata* or *Naringi crenulata* trees on a round slab called a kyauk pyin. The powder is then mixed with water to form a thin yellow paste that is applied directly to the skin. We conducted semi-structured interviews with 25 Burmese persons who wear thanakha. Participants were both men and women, age 12-55, and represented three different regions of Myanmar. Nine distinct dermatologic uses were identified: photoprotection, acne treatment and prevention, skin lightening, skin cooling, aesthetics (make-up), rhytid reduction, pruritis relief, scar reduction, and odor prevention. Our study determined that in Myanmar, thanakha is being used daily for treatment and prevention of some of the most prevalent dermatologic conditions. As travel restrictions to Myanmar diminish, further research should investigate the efficacy and safety of thanakha for various dermatologic conditions.

Hospitalizations for cellulitis in Canada: A retrospective database study

A Baibergenova,^{1,2} A Drucker² and N Shear^{2,1} ¹ Dermatology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada and ² Dermatology Division, University of Toronto, Toronto, ON, Canada

Background: Cellulitis is the most common skin condition responsible for emergency department visits and inpatient admissions in Canada. This study examined hospitalization records of patients admitted for cellulitis in order to determine factors associated with prolonged hospital stay and mortality, as well as health services use by these patients. Methods: Records from the national database of hospital discharges, which encompasses all hospitalizations across Canada, excluding Quebec and the territories, were analyzed. All patients from 2004-2008 with an admission diagnosis of cellulitis (ICD code "L03") were included in the study. Factors associated with mortality and prolonged hospital stay (defined as greater than 7 days) were analyzed in univariate and multivariate analysis through logistic regression and are expressed as odds ratios (OR). Results: During the five-year study period, there were 65,454 patients hospitalized for cellulitis. Majority were males (54%), and the average age at admission was 55.5 years (SD 23.9). Mortality during the admission was about 1%, and the average length of hospital stay was 7.1 days. The most common comorbid condition among patients was diabetes (8.4%), followed by congestive heart failure (3%). Consulting services were used in 39% of hospital admissions. Factors associated with prolonged hospital stay included female gender, advanced age, comorbid congestive heart failure, admission to or consultation by a surgical service, and dermatology consultation (OR 4.5, 95% CI 3.9-5.2). Factors associated with mortality were male gender, advanced age, the presence of any comorbidity, surgical consultation and infectious disease consultation. Interpretation: Cellulitis is responsible for a large number of hospital admissions in Canada. The elderly and patients with comorbidities are at increased risk for longer hospital stay and death. Cellulitis may represent a heterogeneous group of conditions and therefore frequently requires multidisciplinary approach as evidenced by high use of consulting services.

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Designing the 'molluscum contagiosum diagnostic tool for parents' (MCDTP)

JR Olsen,¹ NA Francis,¹ J Gallacher¹ and V Piguet² ¹ Cochrane Institute of Primary Care and Public Health, Cardiff University, Cardiff, United Kingdom and ² Department of Dermatology and Wound Healing, Cardiff University, Cardiff, United Kingdom

Molluscum Contagiosum (MC), a member of the poxvirus family, is a viral disorder of the skin and mucous membranes characterised by discrete, single or multiple flesh coloured papules. The virus can lead to discomfort and pain, in children there can also be symptoms of pruritus, erythema, inflammation and super infections in some cases. Lesions are diagnosed upon sight due to their distinct appearance, in unusual and rare cases they may be referred for biopsy. This study aims to design a self diagnostic tool for parents. A two phased approach was conducted, firstly nine dermatologists were interviewed to establish the key diagnostic features of MC. Interviews were tabulated and grouped by key themes. Medical Illustrations were selected, and dermatologists were asked to choose those which were most representative of typical lesions. The tabulated findings from interviews were then discussed with a patient representative, dermatology specialist and school nurse to produce clear wording in a lay language, also maintaining the key diagnostic elements. The second phase of the study piloted a draft version of the MCDTP at a local parent group (n=10) to determine whether it was clear and understandable. The following themes were identified for the diagnosis of MC; appearance, geographical site, symptoms, and natural history. A colour booklet was produced which used four images, accompanied with key text highlighting the features of MC. The MCDTP is a well designed and piloted tool to allow those without a clinical background to diagnose MC in children. The authors specifically designed this tool as a recruitment aid for a cohort of children over a large geographical area. Before the MCDTP can be used, the diagnostic accuracy of parental use needs to be determined in a validation study against a gold standard assessment. Once validated the MCDTP will also have uses for parents to allow self-diagnosis, and when accompanied with information about MC, may reduce primary care consultations for MC.

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Alcohol intake is associated with increased risk of squamous cell carcinoma of the skin: Prospective cohort study

S Siiskonen,^{1,2} J Han,^{2,3,4} T Li,³ T Nijsten¹ and A Qureshi^{2,3} ¹ Department of Dermatology, Erasmus MC, Rotterdam, Netherlands, ² Clinical Research Program, Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ³ Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA and ⁴ Department of Epidemiology, Harvard School of Public Health, Boston, MA

The objective of this study was to investigate the association between alcohol intake and the incidence of cutaneous squamous cell carcinoma (cSCC). Multivariate Cox survival models with time-dependent exposure and covariates were used to estimate relative risks (RRs) and 95% confidence intervals (CIs) in three separate cohorts of U.S. women and men. The results were then meta-analyzed. A total of 174,998 women and 48,140 men participating in the Nurses' Health Study, Nurses' Health Study II and Health Professionals' Follow-up Study were followed for up to 28 years. Information on alcohol intake and covariates was collected at baseline and updated several times during the follow-up. During a follow-up of 4,234,416 person-years, 2,938 histopathologically verified, incident invasive cSCC and 1,590 cSCC in situ were identified. Alcohol intake was significantly associated with an increased risk of invasive cSCC in all three cohorts. A significant dose-response relationship was observed: each additional drink (12.8 gram of alcohol) per day was associated with 22% increased risk of invasive cSCC (RR 1.22, 95% CI 1.13-1.31) and with 14% increased risk of cSCC in situ (RR 1.14, 95% CI 1.04-1.26). White wine consumption ≥ 5 times a week was significantly associated with an additional risk of invasive cSCC (RR 1.31, 95% CI 1.09-1.59). The results of this large prospective cohort study indicate that even a moderate consumption of alcohol increases the risk of developing cSCC in a dose-dependent manner. Our results are still to be replicated in other large cohorts.

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Excellent reliability and validity of a novel Epidermolysis Bullosa Disease Activity and Scarring Index (EBDASI) compared to two other outcome measures

CH Loh,^{1,6} J Kim,^{1,6} JC Su,² BS Daniel,^{3,6} SS Venugopal,^{4,6} LM Rhodes,¹ L Intong,^{1,6} M Law⁵ and DF Murrell^{1,6} 1 Dept Derm, St George Hospital, Sydney, NSW, Australia, 2 Dept Paeds, Univ of Melbourne, Melbourne, VIC, Australia, 3 Dept Medicine, St Vincent's Hospital, Sydney, NSW, Australia, 4 Dept Derm, Westmead Hospital, Sydney, NSW, Australia, 5 Kirby Institute, Univ of NSW, Sydney, NSW, Australia and 6 Faculty of Medicine, Univ of NSW, Sydney, NSW, Australia

Current outcome measures for epidermolysis bullosa (EB) do not distinguish disease activity from damage, hence they cannot measure changes from interventions well in clinical trials. We aimed to devise an Epidermolysis Bullosa Disease Activity and Scarring Index (EBDASI), which could score activity separately from scarring and to compare its reliability and validity against the Birmingham EB Score (BEBS), using the Physician's Global Assessment Scale (PGA) as a reference measurement. Content validity was established by including all possible physical complications of EB, and the methodology from the previously validated Pemphigus Disease Area Index was adapted to create the EBDASI and piloted on several EB patients. For validation, 16 EB patients (7 EBS, 2 JEB, 5 DDEB, 2 RDEB) were scored separately on the same occasion by five EB experts using the EBDASI, BEBS and PGA scales, each rescoring two patients to assess intra-rater reliability. For inter-rater assessment, the intraclass correlation coefficients (ICCs) for overall total scores were: EBDASI 0.964, BEBS 0.852, and PGA 0.873. For intra-rater reliability, the ICCs and 95% confidence intervals were: EBDASI 0.994(0.976-0.998), BEBS 0.926(0.748-0.981), and PGA 0.932(0.764-0.982). Scatter-plots showed that EBDASI distinguished scores better at lower severities than BEBS and PGA. Bland Altman plots showed that EBDASI had far less intra-rater variability than BEBS and PGA. The EBDASI demonstrated excellent reliability and validity, and was found to be superior to BEBS. As EBDASI measures activity separately from scarring, it should be a very useful outcome measure for trials of novel therapies in EB.

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Development of a disease registry for autoimmune bullous diseases: Initial analysis for the pemphigus vulgaris subset

AA Shah,¹ D Sirois,² V Werth,³ W Zrnchik,⁴ K Seiffert-Sinha¹ and AA Sinha¹ 1 University at Buffalo, Buffalo, NY, 2 New York University, New York, NY, 3 University of Pennsylvania, Philadelphia, PA and 4 IPPF, Sacramento, CA

Pemphigus vulgaris (PV) is a potentially life threatening autoimmune blistering disorder with an incidence of 0.5-5 per 100,000. Collecting large data sets in PV is difficult due to the limited number of patients available for study. There is a need for the development of a unified disease registry to bridge the gaps in knowledge regarding epidemiology, disease manifestation, and treatment outcomes that can be accessed by clinicians and researchers worldwide. In 2010, the International Pemphigus and Pemphigoid Foundation (IPPF) established a web-based disease registry to facilitate the collection of large-scale clinical data, and ultimately biological samples from registry patients for study purposes. We present an initial analysis of clinical data collected from 4/14/2010 – 11/20/2011. A total of 599 patients with autoimmune bullous diseases enrolled, 393 of which had PV. The PV registrants had a female:male ratio of 2.54:1, with an average age at diagnosis of 45.67 ± 14.01 years, a Caucasian majority (73.5%), with most patients living in the US at the time their illness began (77.1%). 215 PV patients reported having lesions at the time of the survey (45% mucosal only, 30% mucocutaneous, and 25% cutaneous only manifestations). PV patients reported a considerable delay in diagnosis after the development of initial symptomatology (>3 months=69.5%; >6 months=36.1%; >12 months=13.5%). 18.8% of patients reported a coexisting autoimmune disease. Of all PV patients, 91 were off therapy, 115 on minimal therapy, and 187 on more than minimal therapy, as defined by consensus guidelines. We found significant differences between male and female patients in their lesion profile, delay in diagnosis, and coexisting autoimmune disease status. This initial analysis highlights the value of a disease registry for epidemiologic data mining and provides a resource for future studies linking basic research data with defined clinical variables.

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Environmental and behavioral risk factors for melanoma among young women in the United States

JE Moreau,¹ LK Ferris³ and DG Winger² 1 University of Pittsburgh School of Medicine, Pittsburgh, PA, 2 Clinical and Translational Science Institute, University of Pittsburgh, Pittsburgh, PA and 3 Dermatology, University of Pittsburgh School of Medicine, Pittsburgh, PA

The incidence of cutaneous melanoma in young women is rising at an alarming rate. To better understand this increase, we sought to identify associations between socioeconomic variables and health behaviors and melanoma severity at diagnosis among women ages 21-39. Cutaneous melanoma data reported by 18 Surveillance Epidemiology and End Results cancer registries (2000-2009) was merged with county-level socioeconomic status (poverty level, household income, high school non-completion) and health behavior (Pap smear use) estimates obtained from the US Census bureau and national health behavior surveys. We used multivariable logistic regression to generate odds ratios (OR) of invasive, non-localized, and >1 mm thick melanoma using county-level estimates, demographic traits, and tumor characteristics as predictors. High school non-completion rate above the US mean was consistently associated with melanoma severity at diagnosis (OR [95% CI] of invasive melanoma: 1.29 [1.18-1.41], non-localized disease: 1.29 [1.07-1.56], and depth >1mm: 1.24 [1.10-1.42]). The same was true for non-white race (OR [95% CI] of invasive melanoma: 1.45 [1.09-1.93], non-localized disease: 1.91 [1.57-2.91], and depth >1mm: 2.09 [1.51-2.92]). Scalp/neck, trunk, and site NOS melanomas were associated with higher odds of invasive melanoma (p<.001), and site NOS melanomas were associated with higher odds of non-localized disease (p<.001). Median income above the US mean was associated with lower odds of invasive melanoma (OR [95% CI]: 0.78 [0.71-0.85]). Pap smear testing rate above the US mean was associated with a lower odds of melanoma >1mm deep (OR [95% CI]: 0.87 [0.78-0.98]). Our results suggest that high school completion is the socioeconomic factor most associated with melanoma severity at diagnosis among women ages 21-39. This information can be used to help improve the design of melanoma prevention efforts targeting this population.

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Dense genotyping of six atopic dermatitis and 180 autoimmune risk loci in 2,425 atopic dermatitis patients

H Baurecht,¹ E Rodríguez,¹ D Ellinghaus,² J Esparza-Gordillo,^{3,4} C Gieger,⁵ S Schreiber,² Y Lee,^{3,4} A Franke² and S Weidinger¹ 1 Department of Dermatology, Allergy, and Venerology, University Hospital Schleswig-Holstein, Kiel, Germany, 2 Institute of Clinical Molecular Biology, Christian-Albrechts-University, Kiel, Germany, 3 Pediatric Pneumology and Immunology, Charité, Berlin, Germany, 4 Max-Delbrück-Centrum (MDC) for Molecular Medicine, Berlin, Germany and 5 Institute of Genetic Epidemiology, Helmholtz Centre Munich, Neuherberg, Germany

Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases, with a polygenic, multifactorial nature. To date, genome-wide association studies have established six susceptibility loci. However, the causal variation at these loci remains unknown. To better define risk variants and identify additional susceptibility loci previously implicated in other autoimmune (AI) diseases, we performed a fine-mapping and association study using 2,425 German AD cases and 5,449 German population controls. All samples were genotyped on the ImmunoChip, a custom high-density array containing 195,806 SNPs and 718 small insertions/deletions across 186 distinct AI risk loci, including the six known AD susceptibility loci and the HLA region. At these loci, the array contains all known SNPs in the dbSNP database, from the 1000 Genomes Project (release of Feb. 2012), and from other AI disease resequencing efforts, therefore providing a powerful means of fine-mapping known AI loci. Following quality control, 128,830 polymorphic markers were available for association analysis. Principal component analysis revealed no marked differences in ancestry between cases and controls. We observed that 132 SNPs within non-HLA risk loci reached genome-wide significance ($P < 5 \times 10^{-8}$) in the screening phase. For each locus, we investigated the existence of multiple independent association signals. Replication of the most strongly associated SNPs ($n=39$) with $P < 10^{-4}$ in 7,196 cases and 15,480 controls from 4 independent case-control sets revealed 6 novel AD risk loci.

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Measuring the severity of topical 5-fluorouracil toxicity

K Korgavkar,^{1,3} M Xiong,^{1,3} K Marcolivio,^{1,2} R Lew,² E Firoz,³ M Weinstock^{1,2,3} and VAKCC Trial Group^{1,2} 1 Dermatoepidemiology Unit, VA Medical Center, Providence, RI, 2 VA Cooperative Studies Program, Boston, MA and 3 Dermatology, Alpert Medical School of Brown University, Providence, RI

The VA Keratinocyte Carcinoma Chemoprevention Trial (VAKCC Trial) evaluates topical 5-fluorouracil (5-FU) for chemoprevention of basal and squamous cell carcinomas. This drug is known to cause cutaneous toxicity including erythema, tenderness, flaking, and crusting/erosions. We sought to develop a reliable scale to measure toxicity from photographs, and to investigate correlation between the scale and patients' self-reports. Photos of 100 participants, about half of whom had applied 5-FU, were reviewed by 3 raters blinded to treatment. A scale, anchored by reference images, was created for erythema and crusting/erosions, the readily visible signs of toxicity. For each pair of raters agreement was assessed using the concordance correlation coefficient (CCC), Pearson correlation coefficients (R), and the weighted kappa statistics (κ). In addition, each participant reported a self-assessment of redness, itching, burning, soreness, crusting/erosions, scaling/flaking, and swelling. Redness and crusting/erosions assessed by the patient were compared to erythema and crusting/erosions from the photographs. For photo grading vs. self-report, values for CCC for erythema and crusting/erosions were 0.35 and 0.55 respectively and values for R were 0.56 and 0.65. For pairwise agreement among 3 raters, values for CCC were 0.84, 0.87, and 0.92, values for R were 0.87, 0.92, and 0.92 and values for κ were 0.65, 0.68, and 0.76. This scale provides a reliable method of assessing severity of topical 5-FU toxicity. Evaluation of toxicity from the photographs also correlates with self-report.

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Predictors of subsequent BCC by body site in the VATTC trial

MY Xiong,^{1,2} MA Weinstock^{1,2,3} and VATTC Trial Group¹ 1 Dermatoepidemiology Unit, VA Medical Center, Providence, RI, 2 Dept. of Dermatology, Alpert Medical School of Brown University, Providence, RI and 3 Dept. of Dermatology, Rhode Island Hospital, Providence, RI

Basal cell carcinoma (BCC) is the most common skin cancer in the United States today, and patients who have had a previous BCC are likely to develop subsequent ones over time. Although risk factors for BCC on the face and ears have been extensively studied, predictors of BCCs on other parts of the body have not. We thus sought to evaluate risk factors for development of subsequent BCC on areas of the body besides face and ears. We studied a high-risk population of 1,131 mostly male, Caucasian, elderly veterans in the Department of Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) Trial. We employed multivariate Cox and logistic regression in order to determine predictors of BCC. We then performed analysis of variance (ANOVA) to explore differences in BCC risk based on body site. There were a total of 335 participants (29%) who developed a BCC on the non-face/ears during the study. The 1, 3, and 5-year cumulative risks of non-face/ears BCC were 11%, 29%, and 41%, respectively. The number of BCCs in the 5 years prior to enrollment was the most important independent predictor for BCCs on the non-face/ears ($p < 0.001$), as it had been for BCCs on the face/ears. In addition, a history of ever use of 5-fluorouracil (5-FU) and occupational sun exposure below age 30 were positive predictors. In contrast, use of ACE inhibitors or ARBs during the study was associated with reduced risk. Age (per decade) was the most important predictor for site of BCC (OR = 1.46, $p = 0.003$ for face/ears vs. rest of body; OR = 1.46, $p = 0.002$ for extremities vs. trunk). The mean ages of BCC on the face/ears, neck, scalp, trunk, and extremities were 72, 72, 69, 68, and 69, respectively. This study documents the key risk factors for subsequent BCC in this very high-risk population.

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Second primary malignancies in patients with history of soft tissue tumors from the SEER database

SH Yu,¹ DE Kurlander¹ and JS Bordeaux^{1,2} ¹ Case Western Reserve University School of Medicine, Cleveland, OH and ² Dermatology, University Hospitals Case Medical Center, Cleveland, OH

We sought to determine risk of subsequent primary malignancies after soft tissue tumor (STT) diagnosis. The Surveillance, Epidemiology, and End Results (SEER) database was used to compare the risk of STT patients developing subsequent primary malignancies (SPMs) compared to the general population. STTs and SPMs were classified according to guidelines provided by the World Health Organization (WHO), which categorized STTs as follows: vascular, perivascular, skeletal muscle, adipocytic, chondro-osseous, fibrocytic/myofibrocytic, so-called fibrohistiocytic, smooth muscle, and uncertain differentiation. Of the 40,697 patients diagnosed with soft tissue tumors, 3,445 developed an SPM. 2835 developed 1 SPM, 253 developed 2 SPMs, and 33 developed 3+ SPMs. Besides second primary STTs, other cancer sites with a significantly increased risk (O:E) were neoplasms of the retroperitoneum (7.88; 95% CI: 4.41-12.99), bones and joints (8.26; 95% CI: 5.24-12.49), melanoma (1.67; 95% CI: 1.40-1.97), and other non-epithelial skin cancers (2.32; 95% CI: 1.42-3.59). The risk of non-Hodgkin lymphoma (extranodal) (11.47; 95% CI: 10.28-12.75) and acute myeloid leukemia (AML) (2.79; 95% CI: 2.07-3.68) was also increased. The risk of developing SPMs was dependent on STT classification, and the risk for each were as follows: vascular (2.68; 95% CI: 2.52-2.85), skeletal muscle (2.26; 95% CI: 1.62-3.08), chondro-osseous (1.72; 95% CI: 1.36-2.14), fibrocytic/myofibrocytic (1.26; 95% CI: 1.07-1.47), uncertain differentiation (1.24; 95% CI: 1.10-1.40), so-called fibrohistiocytic (1.14; 95% CI: 1.05-1.23), and adipocytic (1.10; 95% CI: 1.01-1.19). There was no significant increased risk for developing SPMs after a smooth muscle derived STT (1.03; 95% CI: 0.95-1.12), and none of the secondary neoplasms considered developed after a perivascular STT. This study showed that there was an increased risk of SPM after STT diagnosis and treatment. The excess risk was specific to each secondary cancer site.

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Personal history of prostate cancer and increased risk of incident melanoma in US men

W Li,^{1,2} A Qureshi,¹ A Goldstein,² E Giovannucci,¹ M Stampfer¹ and J Han¹ ¹ Harvard Medical School, Boston, MA and ² National Institutes of Health, Rockville, MD

Steroid hormones, particularly androgens, play a major role in prostatic carcinogenesis. Personal history of severe acne has been associated with an increased risk of prostate cancer. One recent study indicated severe teenage acne as a novel risk factor for melanoma, suggesting a possible relationship between the history of prostate cancer and risk of melanoma. We prospectively evaluated the association between prostate cancer and risk of subsequent melanoma among U.S. men. 42420 participants were included from the Health Professionals' Follow-up Study over a 24-year period. Prostate cancer diagnosis was confirmed using pathology reports. Skin cancers, including melanoma and non-melanoma skin cancer (NMSC), were reported biennially and the diagnosis of melanoma was pathologically confirmed. We calculated the Hazard Ratios (HRs) of melanoma associated with history of prostate cancer. To address the potentially increased surveillance among those with history of cancer, we evaluated the risk of NMSC by history of prostate cancer, as well as risk of melanoma by history of other cancers. We identified 540 melanoma cases from 1986 to 2010. Personal history of prostate cancer was associated with a significantly increased risk of melanoma with multivariate-adjusted HR of 1.81 (95% CI: 1.30-2.50). Although we also observed a slightly increased risk of NMSC by personal history of prostate cancer (HR=1.13, 95% CI=1.05-1.22), the difference in the magnitude of the association between melanoma and NMSC was highly significant (P for heterogeneity=0.006). We did not find an increased risk of melanoma by personal history of other cancers. In conclusion, personal history of prostate cancer is associated with an increased risk of developing melanoma, which may not be due to detection bias. Elevated androgen levels associated with acne may contribute to this association which requires functional studies to clarify.

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Moderate to severe psoriasis is associated with an increased risk of chronic and end stage renal disease

S Wang,¹ J Wan,¹ K Haynes,² D Shin,^{1,2} MR Denburg^{3,4} and JM Gelfand^{1,2} ¹ Dermatology, University of Pennsylvania, Philadelphia, PA, ² Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Philadelphia, PA, ³ Nephrology, The Children's Hospital of Philadelphia, Philadelphia, PA and ⁴ Nephrology, University of Pennsylvania, Philadelphia, PA

Elevated uric acid from high epidermal turnover and chronic inflammation in psoriasis may be toxic to renal tubules. Small studies suggest an increased risk of nephropathy in psoriasis patients. We investigated the risk of chronic kidney disease (CKD) and end stage renal disease (ESRD) in patients with psoriasis via a population-based cohort study using The Health Improvement Network, a large UK medical records database. Subjects 18-90 years old with psoriasis identified by validated medical codes (135,035 with mild, 8,646 with moderate-severe disease as defined by psoriasis treatment patterns) were compared to 716,071 patients without psoriasis, matched on age, practice and time of visit. Previously validated algorithms using medical codes and serum creatinine data were used to define moderate to advanced CKD. In Cox regression analysis, psoriasis was associated with an increased risk of incident CKD after adjusting for traditional risk factors (age, sex, diabetes, hypertension, cardiovascular disease, hyperlipidemia, and body mass index) (hazard ratio (HR): 1.05, 95% CI 1.03 - 1.08). The increased risk was confined to the moderate-severe group (HR: 1.94, 95% CI 1.83 - 2.06) and not observed in the mild group (HR: 1.00, 95% CI 0.97 - 1.02). Patients with moderate-severe psoriasis also had a greater than 4-fold increased adjusted risk of incident ESRD (HR: 4.36, 95% CI 3.04 - 6.25). The findings persisted in multiple sensitivity analyses including when controlling for NSAID use. Our results suggest that moderate-severe psoriasis is a risk factor for developing CKD and ESRD, which has important clinical and mechanistic implications for the research and care of psoriasis patients.

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Milk: An endocrine mTORC1-driving anabolic signal transduction system of mammalian evolution promotes diseases of Western civilization like acne

BC Melnik University of Osnabrück, Dermatology, Environmental Medicine and Health Theory, Osnabrück, Germany

Recent epidemiological evidence points to an association between increased body mass index (BMI) and risk of acne, eczema, psoriasis as well as melanoma and nonmelanoma skin cancer. Increased BMI is the clinical correlate of enhanced activity of the nutrient-sensitive kinase mTORC1 (mammalian target of rapamycin complex 1). Western diet, typically composed of high glycaemic load and high milk and dairy product consumption, is closely linked to high BMI and metabolic aberrations, especially insulin resistance. Milk, the growth-promoting feeding system of mammals, produced by the well-conserved mammalian lactation genome, functions as a signal transduction system driving anabolic mTORC1 signalling. Milk fulfills its biological function by providing highly insulinotropic branched-chain amino acids and its intrinsic ability to raise insulin and IGF-1 plasma levels, which are important activators of mTORC1, the central cellular promoter of cell growth and proliferation and suppressor of autophagy. Age-related diseases of Western civilization have recently been recognized as mTORC1-driven diseases, especially obesity, type 2 diabetes mellitus and cancer. Thus, milk/mTORC1-driven metabolic aberrations may not only play a pivotal role in the pathogenesis of acne but most likely in the development of other common dermatological diseases, especially eczema, psoriasis, and melanoma and nonmelanoma skin cancer.

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Evaluation of AJCC, UICC, and Brigham and Women's Hospital tumor staging for cutaneous squamous cell carcinoma

PS Karia,¹ DP Harrington,² A Jambusaria-Pahlajani,³ GF Murphy,⁴ AA Qureshi¹ and CD Schmults¹ ¹ Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ² Biostatistics, Harvard School of Public Health, Boston, MA, ³ Dermatology, Mayo Clinic, Jacksonville, FL and ⁴ Pathology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Although most cutaneous squamous cell carcinomas (CSCC) have an excellent prognosis, there is a high-risk tumor subset with an increased risk of metastasis and death. However, high-risk CSCC has not been consistently defined, nor associated prognosis estimated. Therefore, clinicians currently have little evidence to guide decisions regarding nodal staging and adjuvant therapy. The current study was undertaken to evaluate the 2010 American Joint Committee on Cancer (AJCC), 2010 International Union Against Cancer (UICC), and 2013 Brigham and Women's Hospital (BWH) tumor (T) staging systems for cutaneous squamous cell carcinoma (CSCC). Primary CSCCs diagnosed 2000-2009 at BWH (n=1,818) were assigned AJCC, UICC, and BWH T stages. Life tables of poor outcomes (local recurrence LR, nodal metastasis NM, and disease-specific death DSD) were constructed and analyzed. In AJCC staging, poor outcomes were clustered in T2 with 72% of LR, 82% of NM, 67% of DSD occurring in T2 cases. In UICC staging, most poor outcomes occurred in T1 and T2 including 81% of LR, 67% of NM, and 50% of DSD. In BWH staging, only 6% of CSCCs were in the upper 2 stages (T2b and T3) but they accounted for the majority of LR, NM, and DSD (53%, 76%, and 83% respectively). While ten year incidences of LR, NM, and DSD were low for low-stage tumors [BWH T1/T2a: 1.3% (1-2%), 0.5% (0-1%), and 0.2% (0-0.5%) respectively], they were significantly higher for high-stage cases [BWH T2b/T3: 23% (16-31%), 23% (16-31%) and 14% (8-21%) respectively]. UICC and AJCC staging for CSCC may be suboptimal as most poor outcomes occur in low T stages (T1 and T2). In BWH staging, the majority of poor outcomes occur in the 6% of tumors that are T2b/T3. These stages define a high-risk group which may be the focus of further study of staging and adjuvant therapy.

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Ten-year publication trends in dermatology in mainland China

S Xin,¹ JA Mauro,² TT Mauro,³ PM Elias³ and M Man^{1,3} ¹ Skin Physiology Res, Dalian Skin Disease Hosp, Liaoning, China, ² Keystone Strategy Grp, Brisbane, CA and ³ Dermatology, VA Med Ctr/UCSF, San Francisco, CA

Background: Since its reform in 1978, China has been experiencing huge changes in many aspects of biomedical research, including dermatologic research. However, how China's economic and intellectual development has affected the publication trends in dermatology, which could mirror scientific development in dermatology and other fields, is unknown. Materials and Methods: In the present study, we analyzed the dermatology publication trends from 2002 to 2011 in mainland China. All data were obtained from www.pubmed.com. Results: The number of publications increased 10-fold over the 10-year period, correlating positively with the increase in gross domestic product per capita during that period. A total of 1,231 articles from mainland China were published in English in 251 journals between 2002 and 2011. A total of 129 journals published only one paper from Chinese departments of dermatology. Over 60% of articles were original research and 21.7% were case reports. Among the journals that published dermatology papers from dermatology departments in mainland China, the most common one was the Journal of Clinical & Experimental Dermatology, which published 5.9% of all papers (73). 2.7% (33) papers were published in the Journal of Investigative Dermatology, the most highly-rated dermatological journal. Conclusions: The results suggest that the number of publications in the dermatological field increased markedly in mainland China over the last 10 years. The dramatic increase in publications can be attributed, at least in part, to significant improvements in economic conditions in mainland China.

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Burden-of-illness in moderate-to-severe psoriasis subjects seeking treatment: An overall descriptive assessment

C. Schaefer,¹ JC Cappelleri,² J Cole,³ S Guenther,⁴ J Fowler,⁵ S Johnson⁶ and C Mamolo² ¹ Covance Inc, Gaithersburg, MD, ² Pfizer Inc, Groton, CT, ³ Covance Inc, San Diego, CA, ⁴ The Dermatology Center of Indiana, Plainfield, IN, ⁵ University of Louisville, Louisville, KY and ⁶ Johnson Dermatology, Fort Smith, AR

This observational study was designed to evaluate the humanistic and economic burden of moderate-to-severe plaque psoriasis (MSPP). Two hundred adult subjects actively seeking treatment for MSPP enrolled in 9 sites in the United States. Consented subjects who met inclusion/exclusion criteria answered questions regarding their disease (e.g., symptoms, treatment, costs) and questionnaires including the SF-12, EQ-5D, Dermatology Life Quality Index (DLQI), and Work Productivity and Activity Index-Psoriasis (WPAI). Results are summarized using descriptive statistics. Of the 200 subjects, 179 (89.5%) had PASI \leq 20, 21 (10.5%) had PASI $>$ 20 (severe); 181 (90.5%) were receiving \geq 1 prescription medication for MSPP; and 120 (60.0%) were treated with a biologic. Mean scores were slightly lower (worse) than the general US population for SF-12 physical component summary (47.7 vs 49.7) and EQ-5D (0.82 vs 0.87), and similar for SF-12 mental component summary (49.54 vs 49.48). On DLQI, 38.5% of subjects reported at least moderate life impact due to MSPP. On WPAI, absenteeism (mean=13.0%) and activity impairment (15.6%) were impacted more than absenteeism (2.0%) due to MSPP. Differences by PASI (\leq 20 vs $>$ 20) in DLQI, overall work, and activity impairment were observed. These findings suggest that relatively normal levels of general health status (SF-12, EQ-5D) can be an achievable goal in this highly treated group of subjects with MSPP. However, in spite of treatment, a number of subjects continue to experience impairment in aspects of functioning (DLQI, WPAI). For subjects whose MSPP makes them compromised (PASI $>$ 20), different treatment options should be explored until better outcomes are achieved. With clearer treatment goals it is likely a higher proportion of subjects could achieve high functional status.

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Mood states and personality traits mediate quality of life impact in chronic pruritus

SP Kini,¹ E Velez,¹ S Booker¹ and SC Chen^{1,2} ¹ Dermatology, Emory University, Atlanta, GA and ² Dermatology, Atlanta Veterans Affairs Medical Center (VAMC), Atlanta, GA

While mood disorders such as depression and anxiety have been considered highly prevalent in patients with chronic pruritus, there is a paucity of epidemiologic data to support these conclusions. Additionally, no studies to date have explored the relationship between the five main personality domains—neuroticism, agreeableness, extraversion, conscientiousness, openness—as they relate to the severity of chronic pruritus and quality of life (QoL) impact experienced by patients. A convenience sample of adults (\geq 18 years) attending the 2012 National Eczema Association (NEA) patient conference and those enrolling via the NEA website were surveyed using the ItchyQoL (itch-specific QoL instrument), Beck Depression Inventory, State Trait Anxiety Inventory, and NEO-Five Factor Inventory (personality assessment) in this cross-sectional study. Multivariate linear regression was performed to determine the impact of these predictor variables on the primary outcome variable, QoL impact of pruritus, at the 0.05 level of significance. Of the 152 subjects surveyed, subjects omitting more than 10% of the total survey responses were excluded. The final 110 subjects were mostly (82%) female, 72% endured symptoms $>$ 10 years and 40% reported their pruritus to be 'severe'. After controlling for disease severity, duration, and demographic factors, depressed mood (4.3, $p < 0.01$), anxiety (1.32, $p = .03$), and the 'neuroticism' personality trait (1.17, $p = .045$) remained significant predictors of greater QoL impact of pruritus. This study highlights that subjects with greater depression, anxiety and neuroticism scores reported greater QoL impact, independent of pruritus severity. It is possible that co-morbid psychological states may contribute to poor coping to itch. Strengthened social support and coping strategies may provide an opportunity to reduce burden of disease in these patients. Further studies incorporating a more generalizable population of itchy patients are indicated.

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Advanced Rai stage and skin cancer tumor stage predicts outcomes of skin cancer in patients with chronic lymphocytic leukemia

NE Velez,³ PS Karia,¹ Y Guo,¹ AR Vartanov,² MS Davids,² JR Brown,² VA Neel³ and CD Schmults¹ ¹ Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ² Medical Oncology, Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA and ³ Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Skin cancer is common in patients with chronic lymphocytic leukemia (CLL). This study sought to determine if progression of CLL, measured by advanced Rai stage (III-IV), is associated with worse skin cancer outcomes. A 20-year retrospective study of adult patients with CLL and skin cancer, excluding basal cell carcinoma (BCC), in two academic centers was conducted. Main outcome measures included hazard ratios (HR) for development of poor skin cancer outcomes (local recurrence, nodal metastasis or death from skin cancer). 135 patients with 381 primary skin cancers were included. Forty-one patients (30%) had an advanced Rai Stage (III-IV) at time of skin cancer diagnosis. Median follow-up from time of CLL and skin cancer diagnosis was 120 and 41 months respectively. Skin cancer diagnoses included squamous cell carcinoma, melanoma, and Merkel cell carcinoma [113 (84%), 20 (15%), and 8 (6%) patients, respectively]. Thirty-seven patients (27%) suffered a poor skin cancer outcome. Risk of dying from skin cancer was equivalent to risk of dying from CLL (13%). On multivariate analysis, advanced Rai stage at time of skin cancer diagnosis and high tumor (T) stage were associated with poor skin cancer outcomes [HR and 95% CI = 4.3 (2.1-11.5) and 5.1 (2.2-8.5), respectively]. The risk of poor outcome was highest (50%; 25-75%) in those with both high T stage and high Rai stage. The risk was elevated as well in those with high T/low Rai (30%; 11-60%), and low T/high Rai (17%; 11-26%). Those with both low T stage and low Rai (I-II) had a low risk of poor outcomes from skin cancer (5%; 3.3-8.9%). In CLL patients with non-BCC skin cancer, mortality is as high from skin cancer as from CLL itself. CLL Rai stage should be considered when risk stratifying skin cancer patients, even in those with low-stage non-BCC skin cancers.

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High compliance but low persistency within 12 months with systemic and biologic treatments for psoriasis in Sweden

A Svedhom,¹ C Mamolo,² J Dalen,¹ JC Cappelleri,² IF Petersson³ and M Stahle⁴ ¹ OptumInsight, Stockholm, Sweden, ² Pfizer Inc, Groton, CT, ³ Orthopedics, Clinical Sciences, Lund University, Lund, Sweden and ⁴ Dermatology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden

The purpose of this study was to analyze treatment patterns of systemic (Syst) and biologic (Biol) therapies for psoriasis (Pso) patients in Sweden. In this retrospective study, a cohort of adults with \geq 1 ICD-10 diagnosis of Pso (L40.X) was identified from two regional registries, Skåne Health Care Register (SHCR) and VEGA, with a combined coverage of 2.8 million people (~30% of the Swedish population). Data included all primary and secondary care visits, and all prescriptions dispensed in Sweden from July 2005 – Sept. 2011 from the National Prescription Registry. Compliance (adherence) was measured as the number of days covered by prescriptions while patients were on treatment divided by the duration (in days) from initiation to discontinuation of treatment. Persistency on treatment covered the duration of time from initiation to discontinuation of treatment; patients were allowed to have gaps between filled prescriptions, but were defined as non-persistent if they had a gap $>$ 60 days (the "grace period"). For Biol therapies, an undesirable treatment effect was defined to occur at (1) up-titration of dosage, (2) augmentation with phototherapy, or (3) subsequent treatment with another Syst or Biol. Patients were highly compliant with both Syst (98%) and Biol (92%) therapy; however, persistency was sub-optimal, with only 54% (Syst) and 55% (Biol) of treated patients classified as persistent within 12 months of initiating treatment. Of the 653 patients treated with Biol, ~30% experienced an undesirable treatment effect within 12 months of initiating treatment. Given the chronic nature of Pso, these findings suggest that many patients with severe Pso may cycle through available treatment options within a few years, highlighting the need for multiple effective treatment options to individualize and optimize life-long pharmacological treatment.

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Bridging dermatologists with patient advocacy groups through smartphones

AS Kourosh,¹ ED Schoenberg, JM DeJace and PR Bergstresser ¹ Department of Dermatology, University of Texas Southwestern Medical Center, Dallas, TX

Patient advocacy organizations in the Coalition of Skin Diseases (CSD) seek to increase their outreach. The heads of CSD organizations reported that less than 10% of their current patient members were referred by physicians, and expressed goals of increasing awareness and patient referrals, especially among young dermatologists, in order to reach and benefit a greater number of patients. The authors created the Skin Advocate iPhone application, which refers patients to appropriate patient advocacy organizations for skin disease and released it as a free download in the Apple application store. The purpose of our study was to determine: (1) whether the Skin Advocate iPhone App would increase physician awareness and referrals to patient advocacy organizations in the Coalition of Skin Diseases (CSD) among Texas dermatologists and dermatology residents and (2) whether it would increase patient registrations among CSD member organizations. Effects were measured subjectively through pre- and post-intervention surveys of Texas dermatologists and residents and objectively through internal analytics that tracked downloads and usage of the iPhone app. Pre- and post-intervention registration numbers for CSD member organizations were also measured. Pre-intervention data for self-reported physician awareness and referral and pre-intervention numbers of registrations for CSD organizations served as historical controls. Our data revealed significant improvement in self-reported physician awareness and referrals and increased patient registrations for the CSD organizations that represented the more common diseases. The Skin Advocate iPhone App improved self-reported physician awareness and referrals to CSD member organizations. We have concluded that an iPhone app that streamlined referrals to patient advocacy organizations for skin disease did improve self-reported physician awareness and subsequent referrals to these organizations and did increase patient registrations for patient advocacy organizations, especially for the more common skin diseases.

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The prevalence of autosomal recessive congenital ichthyosis and of transglutaminase-1 deficiency in Germany: Calculation of estimates using the three-source capture-recapture method

T Hartz,¹ H Hennies,² V Oji,³ I Schmidtman,¹ K Kiekbusch,⁴ B Kleinow,⁴ K Aufenvenne,³ F Uckert¹ and H Traupe¹ ¹ Institute of Medical Biometry, Epidemiology and Informatics, University of Mainz, Mainz, Germany, ² Cologne Center of Genomics, University of Köln, Köln, Germany, ³ Department of Dermatology, University of Münster, Münster, Germany and ⁴ Selbsthilfe Ichthyose, Patient Organization, Mittenwalde, Germany

Except for Spain and Sweden no reliable data are available for prevalence of autosomal recessive congenital ichthyosis (ARCI) in Europe. To overcome this unfortunate situation we calculated estimates of prevalence of ARCI as well as of TG-1 deficient ARCI, making use of three data sources: the national registry of the ichthyosis network NIKK that assembled data on 881 ichthyosis patients (all types), the molecular genetic data base RoughSkin of the Köln center for genomics providing data on 535 patients (all types) and the data base of the German patient organization for ichthyosis (SI) comprising 468 patients (all types). The data were matched using a patient identifier (PID) generator. Prevalence of ARCI was then calculated using the three source capture-recapture method using the log-linear-model. Information on status for TG1-deficiency was taken from the NIKK database (biochemical in situ-monitoring of activity) or from the RoughSkin database (sequencing data). We identified 639 patients diagnosed with ARCI in Germany. This means that the minimum prevalence of ARCI in Germany, having a population of 81.726.000 is 0.78 in 100.000. Applying the capture-recapture method that takes into account that each contributing source is incomplete, we derive a prevalence of ARCI of 1.7 in 100.000 in Germany. For calculation of TG1-deficiency the NIKK data set was used (biochemical data). Here 26 out of 81 investigated ARCI patients exhibited TG1-deficiency meaning that the derived prevalence is 0.5 in 100.000. These numbers are higher than previous textbook assumptions and even exceed the data for ARCI from Spain giving 1.6 in 100.000.

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Low dose aspirin is not associated with a decreased incident skin cancer risk: A population-based cohort study among 1.2 million Dutch inhabitants

LM Hollestein¹, MP van Herk-Sukel², R Ruiter¹, E de Vries^{1,3}, RH Mathijssen¹, EA Wiemer¹, T Stijnen⁴, VE Lemmens^{1,3}, RM Herings², BH Stricker^{1,2} and T Nijsten¹ ¹ Erasmus University MC, Rotterdam, Netherlands, ² PHARMO, Utrecht, Netherlands, ³ Eindhoven Cancer Registry, Eindhoven, Netherlands and ⁴ Leiden University MC, Leiden, Netherlands

Objective: To investigate the protective effect of low dose aspirin use (≤ 100 mg daily) on skin cancer in the Dutch general population. **Methods:** We conducted a population-based cohort study with detailed information on aspirin exposure and cancer incidence using the linkage between PHARMO and the Eindhoven Cancer Registry, including inhabitants between 1998 and 2010 above 18 years and free of cancer at baseline. A Cox model with cumulative low dose aspirin use as a time-varying determinant was used to obtain adjusted hazard ratios (HR). **Results:** We included 1,063,327 non-users and 112,491 new low dose aspirin users with a mean follow up of 9.8 and 11.0 years, respectively. Ever use should not affect skin cancer risk, but was associated with an increased risk of all skin cancers. This could be due to residual confounding and therefore we performed subsequent analyses in new low dose aspirin users. Additional years of low dose aspirin use were not associated with a decreased risk of melanoma (HR per additional year of aspirin use: 1.06, 95% confidence interval [CI] 0.96-1.17), basal cell carcinoma (BCC) (HR 1.07, 95% CI 1.01-1.13) or other skin cancers (mainly squamous cell carcinoma) (HR 1.02, 95% CI 0.99-1.05). Long-term use (>6 years) was also not associated with a decreased risk compared to short-term use (<2 years) for all types of skin cancer (HR melanoma: 1.31, 95% CI 0.61-2.79; HR BCC 1.24, 95% CI 1.00-1.55; HR other skin cancers: 1.92, 95% CI 1.26-2.93). **Conclusion:** Low dose aspirin use was not associated with a decreased risk of skin cancer in the Dutch general population.

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Effectiveness of less commonly used systemic monotherapies and common combination therapies for moderate to severe psoriasis in the real world setting: results from the Dermatology Clinical Effectiveness Research Network (DCERN)

L Takeshita¹, S Wang¹, K Callis Duffin², GG Krueger², AB Troxel¹, AS Van Voorhees¹ and JM Gelfand¹ ¹ University of Pennsylvania, Philadelphia, PA and ² University of Utah, Salt Lake City, UT

Data on the effectiveness of therapies for moderate to severe psoriasis in real world settings remain scant. We recently reported that the effectiveness of commonly used systemic therapies and phototherapy is lower in the clinical setting compared to what is reported in randomized controlled trials. The aim of this study was to determine the effectiveness of less commonly used systemic mono- and common combination therapies for moderate to severe psoriasis. We conducted a cross-sectional study of 371 patients with plaque psoriasis on methotrexate (mtx; reference), acitretin, cyclosporine, infliximab, adalimumab + mtx, etanercept + mtx, or infliximab + mtx at 10 centers in the U.S. The proportion of patients with clear/almost clear skin per Physician Global Assessment differed among treatments: mtx (22.3%), acitretin (35.1%), cyclosporine (36.8%), infliximab (46.3%), adalimumab + mtx (59.2%), etanercept + mtx (50.0%), infliximab + mtx (44.1%) ($p < 0.001$). In adjusted analyses, patients on acitretin (relative response rate 2.01, 95% confidence interval [CI] 1.18-3.41), infliximab (1.93, 95% CI 1.26-2.98), adalimumab + mtx (3.04, 95% CI 2.12-4.36), etanercept + mtx (2.22, 95% CI 1.25-3.94), and infliximab + mtx (1.72, 95% CI 1.10-2.70) were more likely to have clear/almost clear skin compared to patients on mtx, though absolute differences were small. There were no differences in quality of life responses. Patients on infliximab were found to have the longest treatment persistence (median 24 months, interquartile range 7-60), and $>70\%$ were on escalated doses (>5 mg/kg every 8 weeks). Our results, though limited by cross-sectional design, highlight the differences in effectiveness and efficacy of psoriasis therapies and emphasize the need for longitudinal effectiveness studies.

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Severe allergic contact dermatitis to compound tincture of benzoin in post-surgical patients is associated with positive reactions to fragrances and essential oils

J Fetting¹, A Sood², JS Taylor² and D Murray² ¹ Cleveland Clinic Lerner College of Medicine, Cleveland Clinic Foundation, Cleveland, OH and ² Department of Dermatology, Cleveland Clinic Foundation, Cleveland, OH

Compound tincture of benzoin (CTB) is commonly used to increase adherence of adhesive tape to skin after skin incisions in a variety of surgical procedures. There have been case reports of allergic contact dermatitis to CTB; however patients are not routinely patch tested to CTB. A retrospective chart review, including operative reports, was conducted to characterize patients with established CTB contact allergy ($n=7$) in whom aimed patch testing was performed for suspected post-operative dermatitis. Most patients (85%) were female and ranged in age from 25-66 with a mean age of 47; 85% were Caucasian. Four patients had a history of atopy. Each patient underwent a surgical procedure which was followed by a severe blistering rash at the surgical site; some patients had dissemination to other sites. Of the positive reactions to CTB, four were 3+ reactions, two were 2+ reactions and one was a 1+ reaction. Two patients were given antibiotics for presumed infection and four required treated with systemic corticosteroids. Reactions to botanicals, essential oils and fragrances were noted in all patients: five patients reacted to compositae mix 6%, four had a severe 3+ reaction to ylang-ylang oil, four reacted to majantole 5%, and four to peppermint oil. Surgical preparations were also tested. Three patients had 1+ reactions to betadine; none were allergic to chlorhexidine gluconate or Steri-StripsSM. CTB is commonly used in post-operative patients and has the potential to cause severe contact allergy. The lack of knowledge about this compound may cause delay in diagnosis as well as significant post-operative morbidity. Reactions to CTB are usually severe, may require systemic corticosteroid therapy and can be misdiagnosed as post-operative infections. The severe nature of the allergic reactions to CTB may justify recommending that patients who have known allergy to fragrances or essential oils avoid CTB.

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Chronic pruritus and gender: Overview of differences in prevalence in clinic setting, severity and burden of disease

M Weiss and E Weisshaar *Clinical Social Medicine, University Hospital Heidelberg, Heidelberg, Germany*

Chronic Pruritus (CP) (> 6 weeks) is a frequent symptom in dermatology and other diseases, such as internal, neurological and psychosomatic/psychiatric diseases. It goes along with a high burden of disease and impairs health related quality of life in affected patients. The term *gender* is understood to not only include sex differences (biological aspects of women and men) but also regarding social, cultural and psychological aspects of sex. Previous studies have shown statistical magnitudes on CP caused by sex e.g. in prevalence. Although gender has already become an important aspect in medical research, data on gender differences in CP are lacking. For operationalization of gender the variables occupation/professional training were used as they are able to give information about a patient's gender role/social gender uncared of his/her biological sex. Data on patients with CP visiting the itch clinic of the University Hospital Heidelberg from 2008 to 2012 were analyzed. Patients were asked to complete a questionnaire covering occurrence/characteristics of pruritus as well as medical and psychosocial domains including lifestyle variables concerning pruritus. We compared means and frequencies according to sex and gender. A total of 583 patients with CP were eligible for analysis, of whom 55,6% were female. Mean age was 59,0 years (SD: 18,0). There was no pronounced difference between age and gender/sex. 70,6% of the patients had been suffering from CP for 1 year or longer. 53,9% of these were woman. Barely three quarters (73,8%) claimed CP reducing health related quality of life, of these 55,1% were female. Impaired health related quality of life was significantly associated with gender and sex. Severity of pruritus (according to VAS) showed a significant association with only sex. Mean VAS score was 6,55 (SD: 2,4). The collected data allow identifying gender specific outcomes in patients with CP regarding gender identity. First analyses demonstrate the need for improved gender-sensitive patient care to avoid gender blindness.

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Improvement in precision of counting actinic keratosis after annual consensus discussion

KC Lee^{1,3}, R Lew² and MA Weinstock^{1,2} ¹ Dermatoepidemiology, VA Medical Center, Providence, RI, ² Cooperative Studies, VA Medical Center, Boston, MA and ³ Dermatology, Brown University, Providence, RI

Previous studies have demonstrated a lack of agreement in counting actinic keratoses (AKs) among experienced dermatologists. We sought to determine whether cumulative consensus discussions, held yearly for 4 years, could improve agreement among dermatologists counting AKs. A prospective, single-blind study was conducted at 4 VA Medical Centers (Palo Alto, California; Chicago, Illinois; Miami, Florida; Denver, Colorado). Each year, 10 dermatologists met at one of the VA Medical Centers and counted AKs on 3-5 subjects. A consensus discussion was subsequently held to discuss discrepancies in the AK count. After the consensus meeting, dermatologists evaluated 3-5 additional subjects for AKs. The average age of the dermatologists was 47 years old (SD ± 8 years), and their average number of years in practice was 15 (± 9). All subjects were male veterans with marked dermatoheliosis serviced by the dermatology department at a VA Medical Center. Eight subjects were examined during Year 1. Nine subjects were examined during Years 2, and 3. Six subjects were examined during Year 4. There was consistent improvement in the level of agreement among raters during the study period (pre-consensus intraclass correlation coefficient [ICC], Year 1: 0.18, Year 2: 0.27, Year 3: 0.54, Year 4: 0.78, $p=.02$). Post-consensus data was not available for Year 1. Post-consensus ICCs for Years 2, 3, and 4 were 0.53, 0.58, and 0.75, respectively ($p=.01$). These findings suggest that improved precision of counting AKs can be achieved and sustained with yearly consensus discussions.

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Predictors of morpheaform BCC on the face and ears in the VATTC trial

MY Xiong^{1,2}, MA Weinstock^{1,2,3} and . VATTC Trial Group¹ ¹ Dermatoepidemiology Unit, VA Medical Center, Providence, RI, ² Dept. of Dermatology, Alpert Medical School of Brown University, Providence, RI and ³ Dept. of Dermatology, Rhode Island Hospital, Providence, RI

Basal cell carcinoma (BCC) is the most common skin cancer in the United States today, and patients who have had a previous BCC are likely to develop subsequent ones over time. Although BCCs overall are less aggressive than other forms of skin cancer, the morpheaform subtype is particularly concerning due to its benign, scar-like appearance and its ability to spread subclinically. We thus sought to evaluate risk factors for development of subsequent morpheaform BCC on the face and ears. We studied a high-risk population of 1,131 mostly male, Caucasian, elderly veterans in the Department of Veterans Affairs Topical Tretinoin Chemoprevention (VATTC) Trial. We employed multivariate Cox regression in order to determine risk factors for time to first morpheaform BCC. We then performed logistic regression in order to assess risk factors for morpheaform BCC relative to other types of BCC. There were a total of 50 participants (4.4%) who developed a morpheaform BCC during this study. The 1, 3, and 5-year cumulative risks of morpheaform BCC were 1.2%, 4.1%, and 5.4%, respectively. The number of BCCs in the 5 years prior to enrollment was the most important independent predictor of subsequent morpheaform BCCs (HRR=9.71, $p < 0.001$). In addition, a history of ever use of 5-fluorouracil (5-FU) was a positive predictor for morpheaform BCCs (HRR = 2.76, $p = 0.013$), unlike for BCCs in general (though it was for SCCs). Among individuals with morpheaform BCCs, non-morpheaform BCCs, and no BCCs, the proportion of ever-users of 5-FU were 38%, 20%, and 17%, respectively. This study documents the key risk factors for subsequent morpheaform BCC in this very high-risk population. These findings raise concern that BCCs occurring after 5-FU treatment may be more likely to be the morpheaform subtype.

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Lower serum vitamin D levels are associated with increased risk of eczema in US adults

T. Fu, C. Gamba, H. Iwe and JY Tang *Dermatology, Stanford University School of Medicine, Stanford, CA*

Vitamin D's immunoregulatory properties may play a role in development and severity of allergic conditions. Research indicates an inverse relationship between vitamin D levels and severity of eczema in children, and some studies show improved eczema symptoms following vitamin D supplementation and phototherapy. We sought to determine the association between serum vitamin D levels and eczema in U.S. adults. The 2005-2006 National Health and Nutrition Examination Survey included measurement of serum 25-hydroxyvitamin D (25(OH)D) levels and questions about eczema. We used logistic regression to evaluate the relationship between vitamin D levels and eczema status in subjects aged 19-49 years (N=2,839). We categorized subjects as never, ever, and recently having eczema. Serum 25(OH)D levels of <20 ng/mL, 20.1-29.9 ng/mL, and ≥ 30 ng/mL were categorized as deficient, insufficient, and sufficient, respectively. We adjusted for age, race, gender, BMI, season of blood draw, poverty index ratio, milk intake, multivitamin use, television and computer use, physical activity, and sun exposure, and stratified subjects by age group. Overall, vitamin D deficiency was significantly associated with ever having eczema (OR 2.66, 95% CI: 1.47-4.81), and vitamin D insufficiency was associated with recent eczema (OR 2.39, 95% CI: 1.00-5.58) and ever eczema (OR 1.87, 95% CI: 1.10-3.17). Among 19-29 year-olds, vitamin D deficiency was significantly associated with recent eczema (OR 9.57, 95% CI: 1.91-76.95) and ever eczema (OR 6.93, 95% CI: 2.52-19.03), while vitamin D insufficiency correlated with ever eczema (OR 2.77, 95% CI: 0.86-8.86). Trends toward similar associations were also seen in older age groups. Limitations of these results include the survey's cross-sectional nature and self-reporting of eczema diagnosis. In conclusion, vitamin D insufficiency and deficiency is associated with increased eczema risk, especially in young adults. Further investigation on the effects of vitamin D supplementation on eczema in this group is warranted.

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Increasing incidence of bullous pemphigoid in Finland

A. Försti,¹ J. Jokelainen,² M. Timonen² and K. Tassanen¹ *1 Dermatology, University of Oulu, Oulu, Finland and 2 Health Sciences, University of Oulu, Oulu, Finland*

Bullous pemphigoid (BP) is the most common autoimmune blistering skin disease. In studies based on clinical samples the incidence of BP has varied between 2.5-21.7 per 1 000 000 inhabitants per year, however, a British study based on a computerized general practice database reports the incidence of BP as high as 42.8. Moreover, the incidence of BP has been reported to have increased both in UK and France. The aim of our study was to study the incidence of BP in Finland and whether it has increased also in Finland. The study material consisted of all pemphigoid patients diagnosed in the Oulu University Hospital between years 1985-2009. The data of the disease was collected from the patient records. The diagnosis of BP was evaluated with the following criteria: clinical features, histopathological and immunofluorescence (IF) examinations of skin biopsies, indirect IF analysis and BP180-ELISA. The statistical analyses were performed in STATA (Data Analysis and Statistical Software) and PASW (Predictive Analytics Software). 155 BP cases were found. In 92.9 % of the cases BP manifested in the skin and in 7.1 % both in the skin and mucous membranes. The mean age at the diagnosis was 76.7 years. We diagnosed 24, 48, and 83 BP cases between years 1985-1989, 1990-1999, and 2000-2009, respectively. The crude incidence in the Northern Ostrobothnia Hospital District was 16.9 (95% CI 14.5-19.8) / 1 000 000 person-years. Using the European standard population as a reference the age-standardized incidence was 15 (95% CI 12-17) new BP cases per 1 000 000 person-years. The age-standardized incidence rates in five-year periods were 14.0, 12.4, 14.2, 16.5, and 26.8 between 1985-1989, 1990-1994, 1995-1999, 2000-2004, and 2005-2009, respectively. The incidence of BP increased 1.9-fold (IRR 1.9, 95% CI 1.3-2.6) in 2005-2009 compared with the mean incidence level of BP between 1985-2004. In this population-based study with immunohistologically verified BP cases we found that the age-adjusted incidence of BP has increased remarkably in Finland in the end of 2000s.

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Epidemiology of cutaneous lymphoma in Japan: A nationwide study of 1,871 patients

T. Hamada and K. Iwatsuki *Dermatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan*

Most epidemiological surveys on cutaneous lymphomas (CLs) have been limited to case series reports, mainly of single medical centers. Therefore, epidemiologic data of CLs has not been fully evaluated in many parts of the world. To investigate the incidences of various CLs in Japan, using epidemiological data from a nationwide registration system for CLs, and to compare the results obtained from the present study with those from other cohorts. We analyzed the incidence pattern of CLs from 2007 to 2011 in Japan. The present registry covers the entire nation and includes more than 600 dermatological institutes throughout Japan. The 1,871 patients registered included 1,506 (80.5%) patients with mature T-cell and NK-cell neoplasms, 340 (18.2%) with B-cell neoplasms and 25 (1.3%) with immature hematologic neoplasms including 24 with blastic plasmacytoid dendritic cell neoplasm. Mycosis fungoides (MF) is the most common CL subtype in the present study (750 patients, 40.1%). The proportion of MF patients with early-stage disease was 73%, similar to that of previous studies from other cohorts. The incidence rates of adult T-cell leukemia/lymphoma (ATLL) and extranodal NK/T cell lymphoma, nasal type (ENKL) were 15.5% and 1.8%, respectively. The incidence rate of mature T-cell and NK-cell neoplasm in the present study was 3.5 to 9.2% higher than in those of the United States and Europe, because of the high prevalences of ATLL and ENKL in Japan.

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Association between ultraviolet flux and risk of invasive cutaneous squamous cell carcinoma in US men

K. Nguyen,¹ J. Han,^{1,2,3} T. Li² and AA. Qureshi^{1,2} *1 Clinical Research Program, Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, 2 Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA and 3 Department of Epidemiology, Harvard School of Public Health, Boston, MA*

Previous measures of self-reported ultraviolet radiation exposure have been fraught with concerns about recall bias. Ultraviolet flux of residence provides an estimate of ultraviolet radiation exposure on the Earth's surface, serving as a surrogate marker for ambient UV radiation exposure based on an individual's residence history. In this study, we investigated the association between UV flux of residence and risk of invasive squamous cell carcinoma among US men. In particular, we estimated cumulative UV flux as the sum of UV flux to which an individual was exposed based on their reported state of residence. Information on 47,839 male participants with follow-up over 20 years was included from the Health Professionals Follow-up Study. In multivariate models adjusting for known skin cancer risk factors, higher quintiles of cumulative UV flux were associated with an increased risk of invasive SCC in comparison to the lowest quintile (relative risk of invasive SCC: 2.86 (95% CI: 1.52, 5.41) in the highest quintile, p value for trend <0.0001). We also evaluated average annual UV flux and found a similar risk of invasive SCC. In this study, we found a strong dose-response relationship between adult cumulative UV flux of residence and the risk of invasive SCC despite adjustment for all known SCC risk factors.

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Surgical excision versus imiquimod 5% cream for basal-cell carcinoma (SINS): A multi-centre non-inferiority randomised controlled trial

HC. Williams, F. Bath-Hextall, M. Ozolins, G. Colver, W. Perkins, S. Armstrong and P. Miller *University of Nottingham, Nottingham, United Kingdom*

Basal cell carcinoma (BCC) incidence is increasing worldwide. Imiquimod cream may be useful for people with BCC occurring in low-risk body sites, but it has not been compared head to head with standard excisional surgery. We conducted a non-inferiority randomised controlled trial comparing imiquimod 5% cream with surgical excision with a 4mm margin in 501 participants with primary nodular or superficial BCC. Primary outcome was the proportion of participants with clinical evidence of "success", defined as absence of initial treatment failure or signs of local recurrence at 3 years. At 3 years significantly fewer participants in the imiquimod group (83.6%) were successfully treated compared to the surgical group (98.4%), relative risk (RR) 0.84 (98%CI, 0.78 to 0.91), with most imiquimod treatment failures occurring in the first year after treatment. Imiquimod could not be said to be non-inferior to surgery at three years since it did not meet our predefined non-inferiority criterion of RR=0.87. Significantly fewer participants in the imiquimod group were successfully treated compared to surgery at years one and two, RR 0.88 (98%CI, 0.82 to 0.93) and RR 0.86 (98%CI, 0.80 to 0.92), respectively. More participants experienced at least moderate pain during imiquimod treatment compared to surgery whereas less pain was experienced with imiquimod than surgery during the follow-up period. There was no significant difference in cosmetic appearance when rated by participants, but a difference in favour of imiquimod was noted by dermatologists from photographs. There were fewer treatment failures in the surgery group compared with imiquimod and little difference in cost between them. Imiquimod cream may still be a useful treatment option in primary care for small low risk superficial or nodular BCC depending on patient preference.

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Risk of subsequent non-melanoma skin cancers in patients with prior non-melanoma skin cancer

MR. Wehner,^{1,2} E. Lino,¹ R. Parvataneni,¹ SE. Stuart,¹ WJ. Boscardin³ and M. Chren^{1,4} *1 Dermatology, University of California San Francisco, San Francisco, CA, 2 School of Medicine, Stanford University, Stanford, CA, 3 Epidemiology and Biostatistics, University of California San Francisco, San Francisco, CA and 4 Dermatology, San Francisco Veterans Affairs Medical Center, San Francisco, CA*

Patients with non-melanoma skin cancer (NMSC) have increased risk of subsequent NMSCs, but information is limited about the timing and frequency of these subsequent tumors. Our goal was to determine the risk of all subsequent NMSCs and the time interval between NMSC events after the diagnosis of a primary NMSC. We used data from a prospective study of consecutive patients diagnosed with NMSC in 1999-2000 at a university practice or a Veterans Affairs clinic and followed through 2012. We performed multiple-failure analyses using Cox proportional hazards methods with marginal modeling to assess the probability of subsequent NMSC after any primary NMSC diagnosed during the follow-up time. In the 1360 patients, the mean follow-up time was 5.9 years, and 3648 subsequent NMSCs were diagnosed (mean of 0.46 per patient per year). At 1, 2, 3, 5, and 10 years after diagnosis of a primary NMSC, the probabilities of developing a subsequent NMSC were 41.8%, 57.1%, 66.3%, 76.0%, and 85.7% respectively. After adjustment for numbers of dermatology clinic visits and biopsies, increased risk of subsequent NMSC was associated with increasing age, male gender, history of NMSC prior to enrollment, history of HIV infection or organ transplantation, and diagnosis of squamous cell carcinoma or more than one NMSC at enrollment. We conclude that patients with NMSC are at higher risk of subsequent NMSC than previously reported: the risk of an additional tumor is greater than 50% by 2 years and greater than 85% by 10 years after a single NMSC diagnosis. These findings are unique because they include multiple subsequent tumors. They can inform patients and clinicians about prognosis and optimal screening strategies, and they contribute to a growing conception of NMSC as a chronic diathesis with susceptibility to multiple cancers over time.

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Incidence of nonmelanoma skin cancer in patients presenting for routine dermatological care
M Enamandram, KR Donahue, LM Duncan and AB Kimball *Massachusetts General Hospital and Harvard Medical School, Boston, MA*

In light of the significant public health problem posed by skin cancer in the United States, the purpose of this research is to identify the rate of skin cancer diagnosis during routine visits to the Medical Dermatology clinic at Massachusetts General Hospital, a busy urban multi-provider setting. Previously, we found that approximately 9% of patients referred for urgent dermatological care were diagnosed with biopsy proven skin cancer in our urgent access setting for same week appointments. Medical records of patients presenting for routine dermatological care at Massachusetts General Hospital between 03/28/2012 and 09/28/2012 were retrospectively reviewed. All patients diagnosed with nonmelanoma skin cancer histopathologically confirmed by skin biopsy were identified. Billing data was used to identify the number of patients evaluated in Medical Dermatology during the study period. A total of 14,829 unique patients presented for routine dermatological care during the study period. NMSC was definitively diagnosed in a total of 1,251 skin biopsies in 1,038 unique patients (7.0% of the population). 55% of NMSC patients were men and 45% were women, with a mean age of 69.7 ± 13.0 years. Among NMSC identified, 61.8% were basal cell carcinomas, 36.9% were squamous cell carcinomas; 1.3% were other non-melanoma cutaneous tumors. The incidence of NMSC skin cancer in routine general dermatologic care is high and comparable with that observed in our urgent referral setting. Furthermore, the rate of skin cancer is even greater if superficial specimens that limited a definitive diagnosis and melanoma are also included. These findings validate the value of care provided by dermatologists and highlight the likely increasing need for their diagnostic skills as the population ages in the United States.

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Malignancy risk is not demonstrated in patients with immunobullous diseases receiving mycophenolate mofetil

LS Chan^{1,2} and EL Pappo¹ *1 Dermatology, University of Illinois Hospital and Health Sciences System, Chicago, IL and 2 Dermatology, Jesse Brown VA, Chicago, IL*

Increased risk of certain malignancies has been reported in the organ transplant patients who receive immunosuppressants to prevent rejection. However, the same risk in patients with skin diseases receiving immunosuppressants has not been determined. We aim to elucidate whether mycophenolate mofetil (MMF), a common treatment for autoimmune blistering diseases, has an increased risk of malignancy when used in this specific population. Towards that end, billing codes within the university's electronic medical record system were utilized to identify 139 patients who were diagnosed with an immunobullous disease, beginning in 1996 when the hospital first adopted electronic medical records, until 2012, and a chart review was performed. All immunosuppressive drugs, dosages, and duration of use were recorded. Cumulative doses, maximum doses, and average daily doses were calculated. Any development of a malignancy during this time was recorded in detail. Among the 139 patients, 91 used MMF for at least one day, 24 (26.37%) used MMF for more than 4 years, and 13 (14.29%) used MMF for over 5 years. Odds ratios and respective confidence intervals were calculated to compare cancer rates in patients taking MMF for at least 4 years, or those taking MMF for at least 5 years, with patients who were unexposed to MMF. Comparisons were also made between the group using MMF for at least 4 or 5 years and those using MMF for shorter duration or no MMF. Regardless which comparison, all 95% confidence intervals comparing long-duration MMF use to short-duration MMF use or no MMF use included 1.0. Including this number demonstrates no statistical significance between these groups and suggests no relationship or change in odds of a patient having cancer based on duration of MMF use. This small study provides a first analysis for the oncogenic potential of MMF as a treatment for autoimmune blistering diseases and future large studies will help verify potential malignancy risk of MMF and promoting informed treatment decision.

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Hypertension, type 2 diabetes, high cholesterol, related medication use and risk of incident psoriasis in U.S. women

S Wu,^{1,2} W Li,^{1,2} J Han^{1,2,3} and AA Qureshi^{1,2} *1 Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 2 Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA and 3 Department of Epidemiology, Harvard School of Public Health, Boston, MA*

We evaluated whether personal history of hypertension, type 2 diabetes (T2D), high cholesterol, or related medication use is associated with risk of incident psoriasis. A total of 162,051 participants were included from the Nurses' Health Study (NHS, 1996-2008) and Nurses' Health Study II (NHS II, 1991-2005). Information on personal history of physician-diagnosed hypertension, T2D, high cholesterol, and related medication use was collected biennially during follow-up. Relative risks (RRs) of incident psoriasis were estimated using Cox proportional hazards models adjusting for potential confounders. During 2,238,429 person-years of follow-up, a total of 1,034 incident psoriasis cases were confirmed. Hypertension was associated with an elevated risk of psoriasis among those using anti-hypertensive drugs in the combined analysis [multivariate-adjusted RR = 1.32, 95% confidence interval (CI): 1.02, 1.71], and users of beta-blockers were at a higher risk [RR = 1.38, (95%CI: 1.08, 1.75)]. High cholesterol was associated with an elevated risk of psoriasis in the combined analysis [RR = 1.26, (95%CI: 1.06, 1.50)]. T2D was not associated with an elevated risk of psoriasis. In summary, high cholesterol was associated with an elevated risk of incident psoriasis whereas hypertension was only associated with an elevated risk in the presence of anti-hypertensive medication use.

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A market for concierge melanoma clinics may exist

E Seidler,¹ E Vickery,¹ E Jones,¹ E Veledar¹ and S Chen^{1,2} *1 Dermatology, Emory University, Atlanta, GA and 2 Dermatology, Veterans Affairs Medical Center, Atlanta, GA*

Pigmented lesion clinics in academic centers face more demand for visits than they can usually accommodate. Thus, we sought to determine the proportion of such visits that are additional and fall outside of the standard-of-care frequency. We conducted a retrospective chart review from January 2012 to October 2010 and recorded patients' diagnoses, date of diagnosis, follow-up visit schedule for 2 years and demographic information. Based on follow-up schedules per diagnosis, each visit was determined to be "standard" (conform) versus "additional." 609 patients yielded 1,756 visits of which 14.6% qualified as "additional." 56.4% of additional visits were in patients with invasive melanoma; however, 54.8% of all visits were in patients with invasive melanoma. Controlling for diagnosis, the relative frequency of additional visits was similar across all diagnoses: 17% with mild to moderate dysplastic nevi, 23% with atypical mole syndrome, 17% with severely dysplastic nevi or melanoma in-situ, 15% with invasive melanoma and 10% with only a family history of melanoma. There were no significant differences ($p > 0.05$) between patients who had additional visits and those who did not with regards to gender, family history of melanoma, and history of more than one melanoma. These data demonstrate that a concierge market may exist among patients with a history of or risk for melanoma, regardless of severity of disease. In a changing healthcare environment, implementing concierge clinics to accommodate additional visits may serve as an innovative way to meet melanoma patients' needs.

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Basal cell carcinoma incidence and associated risk factors in US women and men

S Wu,^{1,2} J Han,^{1,2,3} W Li^{1,2} and AA Qureshi^{1,2} *1 Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, 2 Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA and 3 Department of Epidemiology, Harvard School of Public Health, Boston, MA*

There is a paucity of data on basal cell carcinoma (BCC) in the United States as most national registries do not collect information on BCC. In this study, the authors described incidence trends and associated risk factors for BCC in 95,743 US women from the Nurses' Health Study (1986-2006), and in 44,428 US men from the Health Professionals' Follow-up Study (1988-2006). A total of 23,943 incident BCC cases were reported during follow-up. Age-adjusted BCC incidence rates increased from 838 cases per 100,000 person-years to 1,322 cases per 100,000 person-years for women, and increased from 727 cases per 100,000 person-years to 1,813 cases per 100,000 person-years for men. Cox proportional hazards analysis identified several strong phenotypic risk factors for BCC in both cohorts: family history of melanoma, blonde and red hair color, higher number of extremity moles, higher susceptibility to burn as a child/adolescent, and higher number of lifetime severe/blistering sunburns (all $P < 0.0001$ for meta-analysis). The multivariate-adjusted risk ratio for the highest quintile versus the lowest quintile of cumulative midrange ultraviolet (UV) flux exposure based on residential history was 3.29 [95% confidence interval (CI): 2.79, 3.88] in men and 1.99 (95% CI: 1.65, 2.40) in women. In summary, the increase of BCC incidence rate was generally higher in men than in women, and BCC risk was associated with several phenotypic and exposure factors including midrange UV radiation.

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Genital psoriasis is associated with significant impairment in quality of life and sexual functioning

C Ryan,¹ MN Sadlier,² M Patel,¹ B Kirby² and A Menter¹ *1 Dermatology, Baylor University Medical Center, Dallas, TX and 2 Dermatology, St Vincent's University Hospital, Dublin, Ireland*

Although genital involvement can have devastating psychosexual implications for psoriasis patients, few studies have examined predisposing risk factors or its impact on quality of life and sexual functioning. This was an observational, multi-center study of 354 consecutive adult patients with psoriasis. Information on patient demographics, clinical severity and phenotype, patient quality of life and sexual functioning was collected. 224 patients (63%) had a current and/or previous history of genital involvement. Of these patients, 87% reported itch, 39% reported pain, 42% reported dysparenia, 32% reported a worsening of their genital psoriasis after intercourse and 43% reported a decreased frequency of intercourse as a result of their genital involvement. Younger age of onset of psoriasis ($p < 0.0001$ for type I versus type 2 psoriasis), more severe disease ($p < 0.0001$ for Psoriasis Area and Severity Index and percentage of body surface area involved), current scalp, nail and flexural involvement were associated with the presence of current genital disease, patients with palmo-plantar involvement were less likely to have a history of genital involvement ($p = 0.003$), while there was no association with joint involvement, circumcision, smoking or obesity. There was strong evidence that patients with current genital psoriasis had a severe impairment in quality of life and sexual health as determined by the Dermatology Life Quality Index ($p < 0.001$), the Center for Epidemiologic Studies Depression Scale ($p = 0.01$) and the Relationship and Sexuality Scale ($p < 0.001$), which was significant in all categories including frequency, quality and fear of sexual relations. The results of this study highlight the psychosexual impact of psoriasis and emphasize the need for dermatologists to systematically screen all psoriasis patients for the presence of genital involvement and the impact of their disease on sexual health.

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Determinants of survival in dermatofibrosarcoma protuberans patients developing subsequent primary cancers

DE Kurlander,¹ JS Barnholtz-Sloan,^{1,3} H Gittleman,³ Y Chen,^{1,3} MR Gerstenblith^{1,2} and JS Bordeaux^{1,2} ¹ Case Western Reserve University School of Medicine, Cleveland, OH, ² Department of Dermatology, University Hospitals Case Medical Center, Cleveland, OH and ³ Case Comprehensive Cancer Center, Cleveland, OH

Recently the research team found patients with dermatofibrosarcoma protuberans (DFSP) to be at increased risk of subsequent primary melanoma, female breast, soft tissue, and other non-epithelial skin cancers, and at decreased risk of colon cancer. This study describes survival of DFSP patients stratified by subsequent primary cancers. Data from the Surveillance, Epidemiology and End Results Program's 9 registries with dates 1973-2009 were used for analysis. Three cohorts were used: Cohort 1, individuals with DFSP and no secondary cancer; Cohort 2, individuals with DFSP with the following secondary cancers: female breast, soft tissue, other non-epithelial skin, colon, and melanoma; and Cohort 3, individuals with DFSP and any other secondary cancer. Kaplan-Meier survival analyses were performed within each Cohort to assess potential survival differences by age at diagnosis, sex, race, and primary site of the tumor. Multivariable Cox proportional hazards models were performed to further assess survival differences adjusting for all factors. For all Cohorts, survival decreased as age at diagnosis increased, in the univariate and multivariate models. For Cohort 1 (N=3459), in the multivariable model black race, male sex, and tumor location on the lower extremity, head, or other site were associated with a significantly increased risk of death. For Cohort 2 (N=131), in the multivariable model black race and tumor location on the genitals were associated with a significantly increased risk of death. For Cohort 3 (N=268), in the multivariable model tumor location on the upper extremity was associated with a significant increased risk of death. Decreased survival by specific key factors is variable for those with and without secondary cancers after DFSP diagnosis. Further analyses will tease out these differences.

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Minimal Clinically Important Difference (MCID) of the Dermatology Life Quality Index (DLQI) scores and responsiveness to change in inflammatory dermatoses

MK Basra,¹ S Salek² and AY Finlay¹ ¹ Department of Dermatology and Wound Healing, Cardiff University School of Medicine, Cardiff, United Kingdom and ² Centre for Socioeconomic Research, School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff, United Kingdom

The aims of this study were to determine the Minimal Clinically Important Difference (MCID) and responsiveness to change of the DLQI in inflammatory skin diseases. This was a longitudinal study; in the first stage patients attending the dermatology out-patient clinic completed the DLQI and a self-assessed disease severity global question (GQ) on a 0-10 visual analogue scale. At the follow-up stage patients completed the DLQI, the GQ and a global rating of change questionnaire (GRCQ) about the change in their overall quality of life (QoL). GRCQ was used as an anchor to measure the MCID of the DLQI scores with a 15-point scoring system (+7 to -7). A total of 192 patients (M=41.7%, F=58.3%) with 20 different inflammatory skin diseases completed the DLQI and GQ at stage 1 while 107 patients completed the DLQI, GQ and GRCQ at stage 2 (mean time interval=71 days). The mean DLQI score of 107 patients at stage 1 was 9.8 (SD=7.8) and 7.4 (SD=7.0) at stage 2 with a mean change of 2.4 (p<0.0001). The ES was 0.3 while the SRM was 0.4, both indicating a small effect according to Cohen's criteria. 31 patients experienced a "small change" in their QoL (± 3 and ± 2) on the GRCQ. The mean corresponding change in DLQI scores was 3.3 (SRM=0.27; ES=0.21) which could be regarded as the approximate MCID of the DLQI scores. The mean DLQI scores in patients with "no change", "moderate" and "large" change on the GRCQ were 2.7 (n=23; SRM=0.01, ES=0.004), 4.4 (n=25; SRM=0.46, ES=0.39) and 6 (n=28; SRM=0.69, ES=0.67) respectively. These findings confirm that the DLQI is responsive to change in patients' QoL over time. Previous estimates of DLQI MCID have varied from 3 to 5; the recommendation from this study is that MCID=3 in inflammatory diseases. This new information is of relevance to the use of the DLQI in clinical research and practice.

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Development and validation of teenagers' Quality of Life (T-QoL) index: A dermatology-specific measure for adolescents

MK Basra,¹ AY Finlay¹ and S Salek² ¹ Department of Dermatology and Wound Healing, Cardiff University School of Medicine, Cardiff, United Kingdom and ² Centre for Socioeconomic Research, School of Pharmacy and Pharmaceutical Sciences, Cardiff University, Cardiff, United Kingdom

The aim of this study was to develop and validate a dermatology-specific quality of life instrument for adolescents with skin diseases. The Classical Test Theory (CTT) and Item Response Theory (IRT) models were employed to develop this new tool and to conduct its psychometric testing. 33 aspects of QoL were identified from semi-structured qualitative interviews with 50 adolescents with skin disease, leading to a 32-item first version of T-QoL. Based on the feedback from 20 adolescents, 2 items were removed resulting in 30-item T-QoL which was then completed by 153 adolescents. Rasch analysis using RUMM 2030 software did not support the validity of the T-QoL as a uni-dimensional measure; factor analysis identified 3 domains. Further 12 items were removed based on Rasch analysis and on CTT, creating the final 18-item questionnaire. Psychometric evaluation was carried out on a new cohort of 203 adolescents (M=115; F=88, mean age=16.2 years). The construct validity of the tool was demonstrated by correlation with Skindex-Teen (r=0.83, p<0.0001), the CDLQI (r=0.75, p<0.001), and the DLQI (r=0.74; p<0.0001). T-QoL showed excellent internal consistency with Cronbach's alpha $\alpha=0.89$ for the total scale score and 0.85, 0.60, and 0.74 for the 3 domains. Similarly, the test re-test reliability was high in stable subjects (n=61) after a mean interval of 7.2 days: Intraclass correlation coefficient (ICC)=0.91 for the total scale and 0.9, 0.76 and 0.74 for the 3 domains. There was a significant change in the total scale score in 41 subjects (mean change=2.46; p=0.02, normal T-QoL score range=0-36) whose skin disease had changed after a mean of 122.5 days (SD=81.2). Built on rich qualitative data from patients, the T-QoL is a simple and valid tool to quantify the impact of skin disease on adolescents' QoL; it could be used as an outcome measure in both clinical practice and in clinical research.

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Personal history of psoriasis and the risk of non-melanoma skin cancers

M Chen,¹ A Qureshi,^{1,2} T Li^{1,2} and J Han^{1,2,3} ¹ Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, ² Channing Laboratory, Brigham and Women's Hospital and Harvard Medical School, Boston, MA and ³ Epidemiology, Harvard School of Public Health, Boston, MA

Background: Some clinical studies have suggested an increased risk of non-melanoma skin cancers among psoriatic patients. However, no large cohort studies have been conducted on personal history of psoriasis and the risk of non-melanoma skin cancers. Objectives: We investigated the association between personal history of psoriasis and the risk of incident non-melanoma skin cancers in a mixed retrospective-prospective cohort design. Methods: We obtained data from three large population-based cohort studies in U.S. women and men. All enrolled participants were followed up to 2008. In a total of 188,406 participants, we identified 3,216 individuals with psoriasis. We calculated relative risks (RRs) and 95% confidence intervals (CIs) of developing non-melanoma skin cancers using logistic regression models. Results: We documented 3,276 incident SCC cases and 19,300 incident BCC cases. Psoriatic patients had a multivariate-adjusted RR of 1.40 (95%CI, 1.09-1.79) for SCC compared with those without psoriasis. The individuals with severe psoriasis are more likely to develop SCC (RR, 1.26 for 3 or more palms of psoriasis; 95%CI, 1.06-1.50; p for trend, 0.01). However, personal history of psoriasis was not associated with the risk of BCC (RR, 1.00; 95%CI, 0.88-1.13). Conclusions: We found that personal history of psoriasis was significantly associated with an increased risk of SCC, but not BCC. Psoriasis may share some common immune pathogenesis with SCC. Certain therapeutic regimens for psoriasis perhaps increase the risk of SCC. Key words: psoriasis, non-melanoma skin cancer.

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Identification of cutaneous T-cell lymphoma geographic hotspots in Houston metropolitan area

IV Litvinov,¹ MT Tetzlaff,² E Rahme,³ P Gangar,⁴ M Tetzlaff,² K Pehr,¹ VG Prieto,² D Sasseville¹ and M Duvic¹ ¹ Dermatology, McGill University Health Centre, Montreal, QC, Canada, ² Pathology, MD Anderson Cancer Center, Houston, TX, ³ Clinical Epidemiology, McGill University Health Centre, Montreal, QC, Canada and ⁴ Dermatology, MD Anderson Cancer Center, Houston, TX

Cutaneous T-Cell Lymphoma (CTCL) is a rare cancer with documented incidence of ~4-8 cases per million individuals per year. Currently the pathogenesis of CTCL remains unknown. Previous case reports suggested that this cancer can occur in married couples as well as cluster geographically and in families, therefore raising a possibility that there might be an important external cause. However, to date there are no documented geographic disease hotspots. In the current work we analyzed the demographic data of 1047 patients from Texas that were seen in a CTCL clinic at the MD Anderson Cancer Center during 2000-2012. Our findings document geographic clustering of patients in a number of communities within the Houston metropolitan area. Furthermore, our results reveal three communities with CTCL incidence rate of 10-50 times higher than the expected rate. In addition, comparison of the disease rate in these communities to the observed rate of CTCL in Texas patients visiting our clinic during 2000-2012 suggests a significant raise after ~2006. In conclusion, identification of geographic clustering combined with the discovery of CTCL disease hotspots strongly argues for the existence of yet unknown external cause in triggering this rare cancer. Identification of additional CTCL hotspots around the world will help identify this trigger and will bring us closer to eradicating death and suffering from this disease.

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Severe teenage acne and breast cancer risk

M Zhang,¹ AA Qureshi,^{1,2} RT Fortner,² SE Hankinson,^{2,3} Q Wei,⁴ L Wang,⁴ H Eliassen,^{2,5} WC Willett,^{2,5,6} DJ Hunter^{2,5,6} and J Han^{1,2,5} ¹ Dermatology, Brigham and Women's Hospital, Boston, MA, ² Medicine, Brigham and Women's Hospital, Boston, MA, ³ Public Health, University of Massachusetts Amherst, Amherst, MA, ⁴ Epidemiology, The University of Texas M.D. Anderson Cancer Center, Houston, TX, ⁵ Epidemiology, Harvard School of Public Health, Boston, MA and ⁶ Nutrition, Harvard School of Public Health, Boston, MA

Background: Acne has been suspected as a result of high levels of circulating androgens, which may increase the risk of breast cancer. We aimed to investigate whether a history of severe teenage acne may predict subsequent risk for breast cancer in our prospective cohort. Methods: We followed 99,128 female nurses for 20 years (1989-2009) in the large well-characterized Nurses' Health Study II cohort. We used Cox proportional hazards models to estimate the relative risks of breast cancer for women with severe teenage acne. We additionally compared the mid-life plasma androgen levels between women with and without a history of teenage acne (n=2,269). Results: During follow-up, 3,303 breast cancer cases were diagnosed. Among women with a history of severe teenage acne, the relative risk was significantly increased for breast cancer (multivariable-adjusted relative risk, 1.17; 95%CI, 1.03-1.32). We confirmed that women with a history of severe teenage acne had higher mid-life free testosterone levels compared to those without (0.17 vs. 0.15 ng/dL, P=0.02). Conclusion: Our results suggest a history of severe teenage acne is a novel risk factor for breast cancer independent from previously identified risk factors. Elevated androgens may contribute etiologically to the observed associations.

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Use of tanning beds and total cancer risk

M Zhang,¹ F Song,² DJ Hunter,^{3,4,5} AA Qureshi^{1,3} and J Han^{1,3,5} ¹ Dermatology, Brigham and Women's Hospital, Boston, MA, ² Epidemiology, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China, ³ Medicine, Brigham and Women's Hospital, Boston, MA, ⁴ Nutrition, Harvard School of Public Health, Boston, MA and ⁵ Epidemiology, Harvard School of Public Health, Boston, MA

Purpose: To investigate the potential health benefits of indoor tanning regarding prevention of internal cancers in the same cohort where we observed increased risks of skin cancers among tanning bed users with a dose-response relationship. **Patients and methods:** We follow 73,358 female nurses for 20 years (1989-2009) in the Nurses' Health Study II and investigated the frequency of tanning bed use during high school/college and at ages 25-35 in relation to the incidence of total cancers (excluding skin cancers). We used multivariate Cox proportional hazards models to estimate the relative risks (RRs) and 95% confidence intervals (CIs) of total cancers and each individual major cancer with more than 100 cases. **Results:** During follow-up, a total of 4,271 internal cancer cases were diagnosed. No association was found between tanning bed use and risk of total cancers (multivariable-adjusted RR, 0.99; 95% CI, 0.95-1.04 for every 4 times/year use on average during high school/college and at ages 25-35). In addition, no association was found for the risk of any individual major cancers, such as breast cancer, thyroid cancer, colorectal cancer, non-Hodgkin lymphoma, or endometrial cancer. **Conclusion:** Our data do not suggest any association between the use of tanning beds and risk of internal cancers. The presumed short-term elevation of plasma vitamin D levels produced by the use of tanning beds does not necessarily translate into risk reduction for internal cancers.

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The need for unified international guidance on HIV dermatology

EE Freeman,¹ R Evans,² T Maurer,⁴ L Muhe³ and P Easterbrook² ¹ Dermatology, Massachusetts General Hospital, Boston, MA, ² HIV Department, World Health Organization, Geneva, Switzerland, ³ Child and Adolescent Health, World Health Organization, Geneva, Switzerland and ⁴ Dermatology, University of California, San Francisco, CA

In the developing world, an area with few practicing Dermatologists, clear guidance is needed on the treatment of HIV-associated skin conditions. In an effort to summarize current national and international guidelines covering HIV Dermatology, a search was undertaken of governmental and professional society guidelines worldwide. Potentially relevant guidelines for HIV-related skin conditions were identified from over fifteen different organizations and national governing bodies, resulting in over forty potentially relevant guidelines published since 1996. For HIV patients, these guidelines addressed adverse HIV-drug reactions, atopic dermatitis, syphilis, HSV, zoster, candidiasis, immune reconstitution inflammatory syndrome, leishmaniasis, HPV, papular pruritic eruption, photodermatoses, impetigo, tinea, warts, molluscum, Kaposi's sarcoma, scabies, eosinophilic folliculitis, and cutaneous tuberculosis. A wide range of decision-making paradigms were employed in the development of these guidelines, ranging from expert opinion to more formalized evidence-based practices such as the Grading of Recommendations Assessment Development and Evaluation (GRADE) process employed by the World Health Organization. Only two guidelines were identified that summarized HIV-associated dermatologic conditions and these were both published in the 1990s. The remaining guidelines were limited in their scope in that they a) were developed for HIV opportunistic infections in general and thereby included some dermatology, b) addressed sexually transmitted infections in general or c) only addressed a very few disease entities. This review identified a gap in up-to-date, evidence based guidelines for HIV Dermatology as a field. The World Health Organization is currently in the process of developing HIV Dermatology guidelines in order to fill this void and provide much needed guidance to those working on the front lines of HIV care.

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Common warts in childhood are associated with increased atopy and infections: A US population-based study

JL Silverberg and NB Silverberg Dermatology, St. Luke's-Roosevelt Hospital and Beth Israel Medical Centers, New York, NY

Little is known about the epidemiology of common warts in the US. We sought to study the US prevalence of warts in childhood and its determinants. We analyzed the 2007 National Health Interview Survey, a cross-sectional study of 9,417 children ages 0-17 years sponsored by the National Center for Health Statistics. Prevalence of warts, demographics, atopic and other infectious diseases were determined. Overall, the US prevalence of childhood warts was 3.3% [95% confidence interval (CI95): 2.8-3.8%]. The prevalence of warts steadily increased between 1-2 and 7-8 years of age, peaked at 9-10 years (8.6% [6.2-11.1%]) and then plateaued at 11-17 years (Rao-Scott Chi-square, P<0.0001). Warts were most common in Whites (P<0.0001), non-Hispanics (P<0.0001) and in households with greater income (P=0.002), higher level of education (P=0.0009) and both parents present (P=0.02). Warts were associated with eczema (logistic regression; P=0.03), hay fever (P<0.0001) and respiratory allergy (P<0.0001), but not asthma or food allergy (P=0.36). Warts were associated with recent history of Strep throat (P<0.0001), other sore throat (P<0.0001), influenza (P=0.004) and sinus infections (P<0.0001) but not recurrent ear infections (P=0.28). These associations remained significant in multivariate models that controlled for age, Race, ethnicity, household income and highest level of education. In summary, there is a significant association between the US prevalence of warts, atopic and other infectious diseases in children. This suggests that barrier and/or immune disruption contributes toward the pathogenesis of warts.

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The role of evidence based dermatology in World Health Organization guidelines

EE Freeman,¹ P Easterbrook,² L Muhe,³ R Hay,⁴ J Martin⁵ and T Maurer⁶ ¹ Dermatology, Massachusetts General Hospital, Boston, MA, ² HIV Department, World Health Organization, Geneva, Switzerland, ³ Department of Child and Adolescent Health and Development, World Health Organization, Geneva, Switzerland, ⁴ International Foundation for Dermatology, London, United Kingdom, ⁵ Department of Epidemiology and Biostatistics, University of California, San Francisco, CA and ⁶ Dermatology, University of California, San Francisco, CA

The World Health Organization (WHO) is in the process of developing HIV Dermatology Guidelines for the first time. A total of 52 HIV-associated dermatologic conditions were assessed for possible inclusion in the guidelines. Inclusion was based on high burden of disease in HIV-infected adults and children, severity of disease or risk of progression, impact on prognosis of HIV, conditions leading to antiretroviral therapy initiation, availability of evidence, applicability for primary health care in resource poor settings, availability of effective interventions, and lack of guidance in currently available guidelines for resource poor settings. A total of 11 cutaneous and 2 oral conditions were selected for potential inclusion. As per WHO protocol, a review was then undertaken of each of these conditions to identify high quality systematic reviews with or without meta-analyses from in the past three years. Data gaps, with lack of up-to-date high quality systematic reviews for HIV patients, were identified for Kaposi's sarcoma, photodermatoses, crusted scabies, eosinophilic folliculitis, papular pruritic eruption, HIV-associated drug reactions, drug resistant HSV, and necrotizing gingivitis. Systematic reviews are being performed to address these identified gaps. The WHO HIV Dermatology guideline process highlights the increasing role of systematic review, meta-analysis, and evidence based decision making in Dermatology. It also underscores the importance of these epidemiologic tools in raising the profile of Dermatologic disease on the world stage.

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Association between severe acne in adolescence and sinopulmonary and gastrointestinal comorbidity: A US population-based study

JL Silverberg and NB Silverberg Dermatology, St. Luke's-Roosevelt Hospital and Beth Israel Medical Center, New York, NY

Little is known about the epidemiology of severe acne in the US. We sought to study the US prevalence, determinants and comorbidities of severe acne in childhood. We analyzed the 2007 National Health Interview Survey from 9,417 children ages 0-17 years. The US prevalence of severe acne was virtually nil in the first decade of life, but increased in a linear fashion from 11 years (1.7% [CI95]: 0.4-3.0%) to 17 years of age (12.1% [7.8-12.5%]) (Rao-Scott Chi-square, P<0.0001). Severe acne was more common in Whites compared with other racial groups at age 14-15 years (P=0.0004) and girls at age 11-13 (P=0.02). Severe acne was associated with increased problems being overweight (multivariate logistic regression, P<0.0001) and comorbid disease. Sinopulmonary disease included sinus infection (P=0.0003), sore throat not due to Strep infection (P=0.0003), asthma (P=0.03), other non-asthmatic lung disease (P=0.03), but not Strep throat/tonsillitis (P=0.07), hay fever (P=0.04) or respiratory allergy (P=0.06). Upper gastrointestinal comorbidities included reflux/heartburn (P=0.0003), abdominal pain (P=0.03), nausea/vomiting (P=0.0001) and food/digestive allergy (P=0.01), but not frequent diarrhea/colitis (P=0.56) or recurring constipation (P=0.09). Psychological comorbidities included depression (P=0.02), anxiety (P<0.0001), attention deficit disorder/attention deficit hyperactivity disorder (P=0.01) and insomnia (P=0.02), but not phobias (P=0.77). In conclusion, there is a significant association between the US prevalence of severe acne, overweight, sinopulmonary, upper gastrointestinal and psychological diseases in children. This suggests that acne may share a common pathogenesis with these disorders.

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The prevalence of alopecia areata among 915,429 dermatology patients seen in dermatology private practice offices throughout the United States

JA Solomon,^{1,2} D Chever¹ and C Caldwell² ¹ Ameriderm Research, Ormond Beach, FL and ² University of Central Florida College of Medicine, Lake Nona, FL

The prevalence of alopecia areata (AA) patients being seen at dermatology practices throughout the United States (US) is unclear. Albeit several reviews have been published, no large review of the prevalence of US patients with AA has been conducted. The largest review of patients published is a Japanese study involving 67,444 patients at 170 clinics. Leavitt Medical Associates of Florida operates or manages 353 dermatology offices involving 915,429 patients seen throughout the US. We undertook a nationwide review to evaluate the prevalence of patients with a diagnosis of AA (ICD-9 code 704.01) presenting to this group of dermatology offices. Corporate billing data was collected in regard to age, gender and diagnosis. Of the 915,429 patients, 82,732 were diagnosed with a hair loss ICD-9 code (091.82, 306.3, 697.0, 704.0 704.00, 704.1, 704.2, 704.8, 757.39, 757.4). Of these, a total of 6,621 patients were diagnosed with AA; equal to 0.7 % of all patients seen, 8 % of patients seen with any hair disorder. Patients with AA ranged from 1 to 98 years of age (yo). Both males (m) and females (f) were distributed over a Gaussian distribution. Nevertheless, males peaked in the 30-39 yo, while females peaked later at 40-49 yo. Of patients 0-10 yo who presented with any type of hair loss, the prevalence of AA was 20.9% m 19.7% f 21.9% . For 31-40 yo 17.9%, m 22.1%; f 15.1%; for 50-59 yo 18.4%, m 13.1% f 21.5%. From these data one cannot determine whether or not the earlier peaking of the male is related to disease incidence or to the decreasing concern among older males with hair loss. AA clearly represents a significant component of patients presenting with hair loss to US dermatology offices with the prevalence varying by age and sex.

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Risk of subsequent cutaneous squamous cell carcinoma in patients with melanoma

MM Asgari,¹ E Warton,¹ C Quesenberry,¹ D Koralek² and M Taylor² ¹ Kaiser Permanente Northern California, Oakland, CA and ² Epidemiology and Patient Reported Outcomes, Genentech, South San Francisco, CA

Melanoma patients are at increased risk of cutaneous squamous cell carcinoma (cSCC), yet the impact of demographic and tumor-related variables on cSCC risk has not been systematically examined. Using a consecutive cohort of melanoma patients diagnosed in a large integrated healthcare delivery system, we examined the incidence rate of cSCC and determined the impact of patient characteristics (age, gender, race/ethnicity) and melanoma tumor characteristics (sequence number, anatomic site, size, stage, and histologic subtype) on cSCC risk. We identified all members of Kaiser Permanente of Northern California (KPNC) diagnosed with a melanoma from 2000-2005 (n=6,378) and obtained data on patient and tumor characteristics and outcomes (cSCC, mortality) from KPNC electronic databases. We calculated incidence rates assuming the Poisson distribution for event counts. Cox proportional hazard models were used to estimate crude and adjusted hazard ratios. A total of 766 subjects developed cSCCs after their initial melanoma diagnosis during follow-up. The median time to cSCC was 2.12 years (mean 2.66, SD 2.22). The overall cSCC crude incidence rate was 2.41 per 100 person-years, and was higher among males (3.10, 95% CI 2.84-3.37) and older subjects. In adjusted models, risk of cSCC was higher among males (HR 1.60, 95% CI 1.37-1.87), older subjects (HR 13.33, 95% CI 8.99-19.77 in subjects >80 compared to <50 years), and non-Hispanic whites (HR 3.30, 95% CI 1.47-7.40). Melanoma characteristics, such as sequence number (HR 1.69, 95% CI 1.26-2.25 comparing 1 to > 3) and anatomic site (HR 1.19, 95% CI 1.01-1.39 sun-protected to sun-exposed) were also associated with cSCC risk. Sensitivity analyses adjusting for outcome definition and cohort entry criteria did not affect our results. In summary, melanoma survivors are at high risk for subsequent cSCC and should be screened with full-body skin check at regular intervals not only for melanoma surveillance, but also for cSCC detection.

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Atrial fibrillation and electrocardiographic characteristics among patients with psoriasis and coronary heart disease

AW Armstrong,¹ S Azizi,² J Wu,¹ C Harskamp,¹ J Farrow,² K Klem,² D Anderson² and EJ Armstrong² ¹ Dermatology, University of California Davis, Sacramento, CA and ² Cardiovascular Medicine, University of California Davis, Sacramento, CA

Psoriasis patients have an increased incidence of cardiovascular disease. Atrial fibrillation is the most common cardiac arrhythmia and is associated with increased morbidity and risk of stroke. The objective of this study is to assess the association between psoriasis and incident atrial fibrillation. Patients with psoriasis who underwent cardiac catheterization were matched to patients without psoriasis at University of California. Electrocardiograms of all subjects were reviewed. The Framingham risk score for atrial fibrillation was calculated to predict incident atrial fibrillation. The subsequent incidence of atrial fibrillation was assessed by chart review with electrocardiographic confirmation. From the 9,473 patients who underwent coronary angiography, 169 patients with psoriasis and no prior atrial fibrillation were identified. When compared to matched controls, psoriasis patients had a higher body mass index (31.5 vs. 29.6 kg/m², P=0.008), but were less likely to have a history of heart failure or hypertension. Patients with psoriasis had a trend towards a decreased predicted incidence of atrial fibrillation (12.8% vs. 14.6% over a ten year period, P=0.06). During a median follow-up of 2.5 years, the observed incidence of atrial fibrillation was similar between cases and controls (Hazard Ratio 0.9, 95% CI 0.5-1.8, P=0.8). Patients with moderate-to-severe psoriasis had a trend towards an increased incidence of atrial fibrillation during follow-up, with a hazard ratio of 2.0 (95% CI 0.5-7.8, P=0.3). Moderate to severe psoriasis may be associated with an increased incidence of atrial fibrillation. Larger studies are needed to confirm this finding.

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Diet and stress perceived to make acne worse in UK teenagers

K Bhate, HC Williams and M Ozolins Centre of Evidence Based Dermatology, University of Nottingham, Nottingham, United Kingdom

Although acne is almost universal amongst adolescents, little is known about their beliefs about which factors that may cause the disease to worsen. We sought to describe the perceptions of a cohort of adolescents with acne about which factors made their acne worse. Adolescents with mild to moderate facial acne taking part in a large clinical trial of commonly used acne treatments in the community were asked the question 'is there anything that makes your acne worse?'. Those responding positively were then asked to elaborate on their perceptions of what worsened their acne using unlimited free text in a study questionnaire. Of the 649 adolescents who took part in the trial, 367 (57%) replied to the question on factors worsening acne, which in turn resulted in 489 itemised responses listing various perceived exacerbating factors including: stress (18.6%), diet (15.1%), facial washes and gels, over the counter (OTC) products (8.8%), menstruation (6.3%) and sweating (6.3%). The most frequent dietary factors perceived to worsen acne were chocolate (3.3%), alcohol (2.7%) and greasy foods (2.7%). This secondary data analysis illustrates the range of factors that adolescents believe can worsen their acne. Stress and dietary components were the factors perceived to worsen acne most commonly in this study. The use of face washes and winter time or cold weather are not commonly cited reasons found in other studies and are worth further investigation. Knowledge of such beliefs helps to identify items that need to be covered in a consultation with a young person with acne so that genuine factors can be explored and myths dispelled. The findings also underline the need to research some of the factors such as diet, stress, sweating, cold weather and wash products more rigorously through epidemiological studies and well designed randomised provocation or prevention studies.

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Journal of the American Academy of Dermatology facebook page posting metrics

R Dellavalle^{1,2} and R Gamble¹ ¹ Dermatology, University of Colorado School of Medicine, Aurora, CO and ² Dermatology, Veterans Affairs Medical Center, Denver, CO

We analyzed user demographic and posting popularity data for the Journal of the American Academy of Dermatology (JAAD) Facebook page on 12/20/2012 to investigate factors promoting audience engagement. The top 5 posts (users reached) with the largest reach were: Heparin reaction! (NEJM Images Physicians should know) (1363), Basal cell carcinoma associated with eczema (1330), Median rhomboid glossitis (NEJM Images in Clinical Medicine) (1,324), Lingual Zoster (NEJM Images in Clinical Medicine) (1,272), Secondary syphilis (NEJM Images Physicians should know) (1267). The top 5 posts (users engaged) with most engaged users were: Tinea (NEJM Images in Clinical Medicine) (212), Median rhomboid glossitis (NEJM Images in Clinical Medicine) (209), Lingual Zoster (NEJM Images in Clinical Medicine) (193), Podoconiosis (NEJM Images in Clinical Medicine) (169), Secondary syphilis (NEJM Images Physicians should know) (166). The top 5 posts (date posted; users talking) talked about were: Scientists discover children's cells living in mother's brains (122), Are you eating enough chocolate? (63), Coffee consumption correlates with less BCC! (61), Tattoo ink infections! (47), J&J removing carcinogens from products (44). Users who "liked" the page were 65% female, with an age distribution of 18-24 years old: 11%, 25-34 years old: 52%, 35-44 years old: 22%, 45-54 years old: 9%, 55+ years old: 4%. The top countries of origin were United States (21%), Brazil (17%) and Egypt (13%). The top languages based on default language settings were English (60%), Portuguese (16%) and Spanish (6%). Links containing clinical case photographs, those related to skin cancer prevention, and correlative studies were well represented among the top posts. Also, the demographics of users that "liked" JAAD's page continue to show an international range of users.

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Epidemiological and clinical characteristics of Behçet's disease in Korea - using a clinical database for patients' registry

S Na,¹ D Kim,² M Cho,² D Bang,² J Roh,³ S Lee¹ and E Lee⁴ ¹ Dermatology, Ajou University, Suwon, Republic of Korea, ² Dermatology, Yonsei University, Seoul, Republic of Korea, ³ Dermatology, Gachon University Gil Medical Center, Incheon, Republic of Korea and ⁴ Rheumatology, Chonnam National University, Kwangju, Republic of Korea

Behçet's disease is a multisystemic inflammatory disorder which shows geographic predominance, specifically in the Far East, such as Korea, China and Japan. This study was planned to establish prospective epidemiologic data of Korean patients as well as diagnostic and therapeutic guidelines through an expert network. On the basis of literature review and analysis, we concluded that further investigation on aggravating factors of Behçet's disease is necessary and other objective scoring systems need to be developed, as subjective indices reported by the individual patient are often exaggerated. Based on the results from the first preliminary registration, we have amended the research protocol and added aggravating factors of the disease. Overall, 36 patients with Behçet's disease mainly from 4 hospitals were prospectively enrolled in the revised protocol. The patients were classified according to the International Study Group (ISG) criteria and revised Japanese classification based on their medical records. The sex ratio was 1:2.6 with female predominance. The incidence among the subgroups was incomplete type 97.2%, complete type 2.8%. Interestingly, 8 people who satisfied Japanese classification did not satisfy the ISG criteria. Clinically, 100% had oral ulcers, 75.0% had genital ulcers, 77.8% had skin lesions and 25.0% had ocular lesions. As for the minor clinical manifestations, joint symptoms were the most frequent. The pathology test was positive in only 9.7% of the patients. Our final aim is to understand the clinical characteristics, natural history and prognostic factors of Korean BD patients through patients' registry for early detection and proper treatment of BD patients.

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An instrument for measuring skin aging in large-scale epidemiological studies holds promise as a monitor for general aging or disease processes

A Vierkötter, L Effner, B Hoffmann, U Krämer and J Krutmann IUF-Leibniz Research Institute for Environmental Medicine, Düsseldorf, Germany

We hypothesize that facial aging reveals dysfunction or disease of internal organs. A previous report, for example, found an association between facial wrinkling and airflow obstruction. The aim of our study was to establish a fast and non-invasive skin aging measurement instrument for large-scale epidemiological studies to investigate the association of skin aging and general aging or disease processes. We tested two different skin aging evaluation instruments in 182 subjects: (1) a skin aging score (SCINEXA) and (2) a digital imaging system (VISIA, Canfield Scientific Inc, USA). By SCINEXA, investigators visually evaluated the severity of skin aging signs like wrinkles and spots. VISIA measures wrinkles and spots quantitatively from photographs. The practicability of the 2 instruments was evaluated according to training effort, inter- and intra-investigator variability, acceptability by investigators and study subjects and costs. The scientific relevance was evaluated by the association of skin aging with chronological age and airflow obstruction (Pearson correlation). Both instruments needed a medium training effort of 2 days, inter-investigator agreement was acceptable for SCINEXA as a deviation of more than 1 score point occurred in only 3% of all evaluations but was not acceptable for VISIA as standard deviations were too high for all evaluated signs except wrinkles. The intra-investigator variability was acceptable for SCINEXA (no deviation of more than 1 score point) but not acceptable for VISIA (standard deviations too high except for wrinkles). Both instruments had a high investigator/subject acceptability, both have short subject assessment times, SCINEXA is much cheaper than VISIA and finally, SCINEXA showed significant associations with age (p<0.0001) and airflow obstruction (p=0.002) and VISIA only with age (p<0.0001). In conclusion, we would recommend SCINEXA as a suitable skin aging evaluation instrument.

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How to retrieve acceptable scores from DLQI: An introduction to Rasch measurement using the DLQI in a sample of hand eczema patients

RF Oienloch,¹ TL Diepgen,¹ P Elsner,² E Weisshaar¹ and C Apfelbacher³ ¹ Clinical Social Medicine, University Hospital Heidelberg, Heidelberg, Germany, ² Department of Dermatology, University Hospital Jena, Jena, Germany and ³ Medical Sociology, Institute of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany

The dermatology life quality index (DLQI) is the most commonly used dermatology-specific health-related quality of life (HRQOL) measure. In recent years the psychometric properties of the DLQI have been a subject of debate as principles of modern test theory seem to be violated. It has been concluded that the use of the DLQI in psoriasis and atopic dermatitis patients cannot be recommended anymore. The aim of this study was to test whether those violations also occur in patients with hand eczema. We collected data of 602 hand eczema patients who participated in an inpatient dermatology rehabilitation program in Germany. In order to report meaningful scores of the DLQI, data was analyzed according to the principles of Rasch measurement, including threshold order, fit statistics and differential item functioning (DIF) which was used to assess the impact of centre, gender and age. We found 8 items showing DIF and 2 items with disordered thresholds. Overall the DLQI showed significant misfit to the Rasch model ($p < 0.001$). We successfully calibrated the DLQI according to the Rasch model by applying a general algorithm. Items were rescored or removed from the scale resulting in a 6 item version with a range from 0-15 points. This version showed no significant misfit to the Rasch model ($p > 0.14$). The results were replicated in another sample of hand eczema patients ($n = 511$). We conclude that the use of the DLQI to assess HROQL in hand eczema patients cannot be recommended anymore. If done already the alternative scoring procedure as presented in this work is recommended for analyzing data. Researchers using the DLQI in other skin diseases should test the fit of their data according to the principles of modern test and calibrate the DLQI before reporting results in case of misfit.

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High incidence of striae distensae in pediatric adolescent patients on high dose corticosteroids for treatment of rheumatic disease and effect on adherence to prescribed regimen

NT Washington¹ and AS Chang² ¹ Department of Pediatric Rheumatology, Lucile Packard Children's Hospital at Stanford University, Palo Alto, CA and ² Department of Dermatology, Stanford University Hospitals and Clinics, Palo Alto, CA

The appearance of striae distensae (SD) in adolescent patients within the first three months of high dose corticosteroid treatment for rheumatic illness has not been reported. Furthermore, the effect of these scarring lesions on medication adherence is unclear and could have significant consequences if non-adherence resulted in life-threatening organ damage. The purpose of this prospective observational study is to assess whether the development of SD during high dose steroid therapy affects drug adherence in pediatric rheumatic diseases. After institutional review board approval, we enrolled participants aged 10-21 years at onset or flare of a systemic autoimmune disease. Subjects underwent treatment with high dose corticosteroids (1-2mg/kg/day) and were assessed monthly for the development of SD in the axilla, breast, arm, abdomen, back, hip/buttocks, thigh, knee, and calf. SD were scored by the treating physician for severity and participants completed the Medication Adherence Self Report Inventory (MASRI), a validated patient adherence tool. A high rate of SD developed within the first 3 months of high dose steroid treatment (8 out of 11 participants, 72%). Most frequent sites of SD development were: abdomen (55%), back (55%), and thighs (55%). 80% of participants reported embarrassment, self-consciousness or sadness due to SD; 40% reported pain, soreness or pruritus with SD. One of 11 participants who developed SD reported less than complete adherence. Additional studies with larger sample sizes will shed light on the effect of SD development and adherence to high dose corticosteroid regimen during the initial, and most crucial time of patients' diagnoses.

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Ethnic and racial disparities in the use of office-based dermatology visits among the insured, 2005-2010

VM Harvey,^{1,2} J Paul,³ V Beresovsky⁴ and L Boulware⁵ ¹ EVMS, Norfolk, VA, ² Hampton University, Hampton, VA, ³ Virginia Clinical Research, Norfolk, VA, ⁴ NCHS, Hyattsville, MD and ⁵ JHU Bloomberg School of Public Health, Baltimore, MD

Objective: Using data from the National Ambulatory Medical Care Survey, we explored ethnic and race differences in the utilization of insured office-based dermatology visits in the US. Methods: In weighted multivariable models providing national estimates, we explored trends in the magnitude of ethnic/race disparities in dermatology visits and referrals among patients with public and private insurance from 2005-2010. Results: 190,612,400 visits occurred among those with public (Medicaid/Medicare or Medicaid/State Children's Health Insurance Plan) or private insurance. The proportion of dermatology visits attended by minorities remained largely unchanged overall, but increased among privately insured Hispanics (from 1.3% in 2005 to 4.8% in 2010, p trend=0.003). Individuals with public insurance were statistically significantly less likely to visit dermatologists compared to those with private insurance (odds ratio (OR) [95% Confidence Interval (CI)] 0.46 [0.39-0.55]). Privately insured non-Hispanic Blacks (NHB) and Hispanics had significantly lower odds of attending visits compared to privately insured non-Hispanic Whites (NHW) (OR [95% CI] 0.61 [0.39-0.94] and 0.47 [0.35-0.62] for NHB and Hispanics, respectively). NHB and Hispanics with public insurance also had lower odds of attending dermatology visits compared to NHW (OR [95% CI] 0.38 [0.24-0.62] and 0.45 [0.26-0.80] for NHB and Hispanics, respectively). Referred visits occurred at equal rates among minorities compared to non-minorities, while non-referred visits were statistically significantly less likely to occur among minorities regardless of insurance type. Conclusion: Insured minorities attended dermatology visits less frequently than their non-minority counterparts; disparities were primarily confined within non-referred visits suggesting that system-related (scarce workforce) and patient related (preferences) factors contribute to disparities in the use of dermatologic services.

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Dynamics of the incidence of cutaneous T-cell lymphomas in Moscow

N Potekae,^{1,2} L Khamaganova,¹ A Almazova,² G Lebedeva,² V Lysenko² and O Shvec² ¹ department of skin diseases & cosmetology, Russian national research medical university named after N.I. Pirogov, Moscow, Russian Federation and ² Moscow research & practical centre for dermatology & cosmetology, Moscow, Russian Federation

Cutaneous T-cell lymphomas (CTCL) are the most common primary skin lymphomas. They are characterized by clonal proliferation of malignant CD 4+ skin-homing lymphocytes. The most common subtypes are mycosis fungoides and Sézary syndrome. The incidence rate is discussed. Objective of the study was to assess the incidence of CTCL in Moscow for the last four years. Methods: calculation & statistical manipulation. Results: the total amount of skin diseases was 300540 including 47 cases of CTCL in 2008; 322323 including 52 cases of CTCL in 2009; 354264 including 33 cases of CTCL in 2010; 503068 including 17 cases of CTCL in 2011. There was revealed the tendency to decrease the incidence of CTCL ($p = 0.06$). However, we can not propose the real decline of the incidence of CTCL. It is well known that the early lesion in CTCL resembles both clinical & histological benign inflammatory disorders with hyperproliferative epidermis with infiltration of T-cells & some cases might be misdiagnosed. On the other hand, there is no evidence of the decrease of the influence of the provocative agents (viral infections, immunosuppressive therapy etc.) on the development of CTCL. We did not reveal any reliable changes in examining the incidence of Kaposi's sarcoma (KS), which is known to have some predisposing factors similar to those in CTCL. KS was diagnosed in 22 cases in 2008, in 29 in 2009, in 28 in 2010, in 19 in 2011. The present study shows that it is necessary to continue the study of the incidence of CTCL.

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Trends in social media use among dermatology journals

R Gamble,¹ B Gilchrist² and R Dellavalle^{1,3} ¹ Dermatology, University of Colorado, Aurora, CO, ² Dermatology, Boston University, Boston, MA and ³ Dermatology, Veterans Affairs Medical Center, Denver, CO

In order to track the role of social media in medical information transfer, we analyzed postings on Facebook and Twitter sites for 102 dermatology journals on 5/30/12 and again 6 months later for the 10 most frequently posted journals. Facebook likes increased by 1,866 (53%) with up to 3007 for the most popular (JAAD) and included the first (JID) and third (JAAD) highest ISI impact factor journals. Most liked journals (no. Facebook likes 5/30/2012 vs. 1/1/13, ISI Impact Factor), were: 1. J Am Acad Derm (1747 vs. 3007 likes, 4.0), 2. Arch Derm (716 vs. 972 likes, 3.9), 3. J Clin & Exper Derm Res (589 vs. 796 likes, 1.1 unofficial), 4. J Derm Nurse Assoc (266 vs. 369 likes, n/a), 5. Cutis (172 vs. 212 likes, 0.5). Tweets were similar in absolute numbers and increases over 6 months but 3 of the 5 most active accounts were for non ISI-ranked publications. Dermatology journals and news services (no. Twitter followers 5/13/12 vs. 1/1/13, ISI Impact Factor) tweeting were: 1. Derm Times (3069 vs. 4272 followers, n/a), 2. Arch Derm (2,283 vs. 3007 followers, 3.9), 3. Derm Online J (1488 vs. 1890 followers, n/a), 4. Cosmet Derm (393 vs. 716 followers, n/a), 5. J Derm Nurse Assoc (343 vs. 1749 followers, USA, n/a). About 10% of dermatology journals actively post on Facebook or Twitter, and 80% of these are US-based compared to 15% of all SCImago dermatology journals. JID (+1615) and J Derm Nurse Assoc (+1406) had the greatest absolute increases on Facebook and Twitter respectively. Dermatology journals on Facebook on average had about twice the impact factor of those tweeting (ISI 1.9 vs 1.0). The data suggest modest but increasing use of social media among readers of medical journals, with Facebook use predominating among the higher-ranked.

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Risk factors and genetics of sagging eyelids in Europeans

LC Jacobs,¹ F Liu,² I Bleyen,³ DA Gunn,⁴ A Hofman,⁵ CC Klaver,^{3,5} AG Uitterlinden,⁵ TD Spector,⁶ M Kayser² and T Nijsten¹ ¹ Dermatology, Erasmus MC, Rotterdam, Netherlands, ² Forensic Molecular Biology, Erasmus MC, Rotterdam, Netherlands, ³ Ophthalmology, Erasmus MC, Rotterdam, Netherlands, ⁴ Unilever Discover, Sharnbrook, United Kingdom, ⁵ Epidemiology, Erasmus MC, Rotterdam, Netherlands and ⁶ Twin Research and Genetic Epidemiology, King's College, London, United Kingdom

Sagging eyelids are a frequent cosmetic concern in the elderly, while risk factors are largely unknown. Sagging eyelid skin shows the same features as normal aged skin, suggesting a shared aetiology. In this study we investigate the contribution of exposure to environmental influences and the genetic predisposition towards developing sagging eyelids. Sagging status was graded for 5,578 Dutch Europeans using digital eye photographs (mean age 67 years, N case = 993) and for 2,186 UK twins using digital portrait photographs (mean age 53 years, N case = 344, N monozygotes = 1,006). Potential risk factors including aging, gender, smoking, severe sunburn, skin color, BMI and hormonal status were examined for association with sagging status in the Dutch individuals using multivariate logistic regression. We estimated the heritability of sagging eyelids in UK twins. Furthermore we conducted a genome-wide association study (GWAS) searching for single nucleotide polymorphisms (SNPs) associated with sagging status in both the Dutch and UK individuals. We identified age (OR=1.02 per year; 95%CI=1.01-1.03), male gender (OR=1.48; 95%CI=1.28-1.70), current smoking (OR=1.28; 95%CI=1.08-1.51) and light skin color (OR=1.24, 95%CI=1.07-1.44) as significant and independent risk factors for sagging eyelids. Heritability was estimated to be 57%. Our GWAS revealed SNPs at ten loci associated with sagging status with suggestive evidence ($5 \times 10^{-8} < P < 1 \times 10^{-5}$), indicating *EPHA8*, *SMYD3*, *KCNQ5*, *RIMS2*, *MYOF*, *BLNK*, *CDK17*, and *DLCAP1* as candidate genes potentially involved in the development of sagging eyelids. This is the first observational study demonstrating that in addition to age and gender, skin color, smoking, and genetic variants are important factors in the aetiology of skin sagging.

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Varying prevalence of depression in psoriasis according to assessment method: a systematic review and meta-analysis

EA Dowlathshahi,¹ M Wakkee,¹ L Arends^{2,3} and T Nijsten¹ ¹ Dermatology, Erasmus Medical Centre, Rotterdam, Netherlands, ² Biostatistics, Erasmus Medical Centre, Rotterdam, Netherlands and ³ Institute of Psychology, Erasmus University, Rotterdam, Netherlands

Psoriasis patients suffer from impaired Health Related Quality of Life but also show signs of depressive symptoms. This study aims to compare depression in psoriasis patients to healthy controls, to determine the prevalence of depression in psoriasis and to investigate how the method of assessment of depression can affect this prevalence. We conducted a systematic literature search on psoriasis and depression in several databases. We compared mean values for depression questionnaires between psoriasis patients and controls to obtain pooled Standardized mean differences (SMD) and 95%CI, and depression rates according to questionnaires, antidepressant use, International Classification of Diseases (ICD) and the Diagnostic and Statistical Manual of Mental Disorders IV (DSMIV) obtaining pooled OR. Further, we pooled mean values and proportions of depressed psoriasis patients according to the different assessment methods. We included 100 studies, mostly conducted in tertiary centres with only few population based studies. According to studies using questionnaires to assess depression, psoriasis patients were significantly more depressed than healthy controls with a SMD of 1.16 (95%CI 0.67-1.66). Five population based studies showed that psoriasis patients had 1.6 higher odds of a depression according to the ICD than healthy controls (95%CI 1.40-1.76) and also used more antidepressants (OR 4.24, 95%CI 1.53-11.76). The majority of the studies included psoriasis patients without a healthy control group (n=73) and reported varying pooled rates of depression in psoriasis depending on the assessment method: 28% for questionnaires, 12% using the ICD, 19% using the DSMIV and 9% for antidepressant use. Psoriasis patients show more signs of depression than their healthy peers. Interestingly, the prevalence of depression in psoriasis varies between 9-28% and is highest when questionnaires are used to assess depression and lowest when antidepressant use is measured.

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A pilot study using unannounced patients and moulage to measure melanoma detection rates by internal medicine residents

C Hernandez¹ and JK Robinson² ¹ Dermatology, University of Illinois at Chicago, Chicago, IL and ² Dermatology, Northwestern Feinberg School of Medicine, Chicago, IL

Melanoma outcome disparities in skin of color have been attributed in part to low levels of primary care physician training in its presentations. Unannounced standardized patients (SPs) are actors placed in physicians' practices to evaluate their behavior in a real clinical setting. This pilot study tested the feasibility of using unannounced SPs and moulage (a mock clinical finding applied to the SP) to determine internal medicine (IM) resident physicians' melanoma detection rates for White and Black SPs. Eight unannounced SPs, 4 White and 4 Black were evaluated by 8 third-year University of Illinois at Chicago IM residents. Two White and 2 Black SPs had a melanoma moulage applied to the hypothenar eminence on the palm (hand) while 2 White and 2 Black SPs had the moulage placed on arch of the sole (foot). Each group of SPs presented with a clinical scenario that should prompt either a hand or foot examination. SPs were instructed not to point out the melanoma. SPs audio-recorded their visits and documented whether the moulage was detected or not. Of the 8 unannounced SPs evaluated only 1, a White SP, had the moulage detected on the foot. SP recordings were content-analyzed using the Inventory of Diagnostic Thinking Processes (DTP) from the Gale and Marsden model for clinical decision-making. This model describes specific decision-making processes that occur as a physician attempts to solve a clinical problem and assists in determining the source of diagnostic errors. The most common DTP was "failure to make a specific enquiry" since (7/8) residents failed to ask about the moulage. Melanoma detection rates for both Whites and Blacks were low in the pilot study and it begins to highlight the need for greater emphasis on the clinical skin examination in medical education. Early detection remains one of the most important interventions for melanoma. The failure of residents to notice the atypical lesion represents a lost opportunity to provide an intervention for their patients.

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Herpes zoster vaccine effectiveness against incident herpes zoster and post-herpetic neuralgia in an older US population

SM Langan,¹ L Smeeth,¹ DJ Margolis² and SL Thomas¹ ¹ Dept of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London, United Kingdom and ² Dept of Dermatology, University of Pennsylvania, Philadelphia, PA

Herpes zoster is common with serious consequences, notably post-herpetic neuralgia. Vaccine efficacy against incident zoster and post-herpetic neuralgia has been demonstrated in clinical trials, but effectiveness has not been studied in unselected general populations. It is critical to establish vaccine effectiveness in a population unrestricted by region, full insurance or immune status. Our objective was to assess zoster vaccine effectiveness in a general population-based setting. A cohort study of 766,330 fully eligible individuals aged ≥65 years was undertaken in a 5% random sample of Medicare who received and did not receive zoster vaccination between 2007 and 2009. Incidence rates and hazard ratios for zoster and post-herpetic neuralgia were determined in vaccinated and unvaccinated individuals. Analyses were adjusted for age, gender, race, low income, immunosuppression and important comorbidities associated with zoster, and then stratified by immunosuppression status. Vaccine uptake was low (3.9%) particularly among black people (0.3%) and those with evidence of low income (0.6%). 13,112 US Medicare beneficiaries developed incident zoster; the overall zoster incidence rate was 10.0 (95% CI 9.8-10.2) per 1,000 person-years in the unvaccinated group and 5.4 (95% CI 4.6-6.4) per 1,000 person-years in vaccinees, giving an adjusted vaccine effectiveness against incident zoster of 0.48 (95% CI 0.39-0.56). In immunosuppressed individuals, vaccine effectiveness against zoster was 0.37 (95% CI 0.06-0.58). Vaccine effectiveness against post-herpetic neuralgia was 0.59 (95% CI 0.21-0.79). Vaccine uptake was low with variation in specific patient groups. In a general population cohort of older individuals, zoster vaccination was effective against incident zoster, including among those with immunosuppression. Importantly, our study is the first to fully examine and demonstrate vaccine effectiveness against post-herpetic neuralgia.

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Thymic stromal lymphopoietin (TSLP) and atopic dermatitis (AD) in a longitudinal cohort

DI Margolis, B Kim, AJ Apter, J Gupta and N Mitra University of Pennsylvania School of Medicine, Philadelphia, PA

TSLP is a master initiator of allergic inflammation. In 2010, a study showed a decreased risk of AD among children with TSLP rs1898671 variant. The goal of our study was to determine if TSLP genetic variation was associated with AD persistence and whether it modified the effect of FLG loss of function mutations in a white cohort. We assessed associations assuming an additive genetic model and a mixed effects logistic regression. Genotyping for 14 tag SNPs in TSLP and for the four most common European FLG mutations was performed using a custom Illumina Goldengate SNP chip (Illumina, San Diego, CA) and TaqMan® assays, respectively. Clinically, 429 white children from the Pediatric Eczema Elective Registry (PEER) were evaluated every 6-months for an average of 5.7 (±1.4) years. Only rs1898671, with a minor allele frequency of 0.225 was associated with an increased likelihood of a child reporting no symptoms of AD (Odds ratio (OR): 1.72, 95% CI: (1.11, 2.65)) during follow up. This association was minimally changed when the model was adjusted for gender, presence of FLG mutation, and age of onset of AD (1.68 (1.09, 2.59)). Previously, FLG mutations were associated with an increased persistence of AD among this white subcohort of PEER. However, in this study, among those with FLG mutations, rs1898671 appeared to reverse this effect. Those with FLG mutations and the rs1898671 variant had less persistent AD as compared to those with FLG mutations only (5.68(2.18, 14.82)). While FLG mutations result in a more porous skin barrier, TSLP likely promotes the immune response to antigens that breach the defective barrier. These findings provoke the hypothesis that rs1898671 or a variant in linkage disequilibrium may diminish TSLP activity thereby decreasing cutaneous inflammation and allergy. Further investigations, including fine-mapping and functional investigations, need to be conducted in order to determine the causal variant.

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Epidemiology of anorectal melanoma in the United States: 1992-2009

A Callahan,¹ WF Anderson,² S Patel,^{1,3} JS Barnholtz-Sloan,^{1,4} JS Bordeaux,^{1,3,4} MA Tucker² and MR Gerstenblith^{1,3,4} ¹ Case Western Reserve University School of Medicine, Cleveland, OH, ² Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Rockville, MD, ³ Department of Dermatology, University Hospitals Case Medical Center, Cleveland, OH and ⁴ Case Comprehensive Cancer Center, Cleveland, OH

Anorectal melanoma is a rare type of malignant melanoma that is not well-characterized. We, therefore, used the National Cancer Institute's Surveillance, Epidemiology, and End Results 13 Registries Database (SEER) to analyze anorectal melanoma in men and women from 1992 through 2009. There were 228 anorectal melanoma cases with nearly 689,657,439 person-years of follow-up. Most of the cases occurred in the rectum (38.6%). Incidence rates were highest among white women ages 75-84 years; 0.30 per 100,000 (95% CI: 0.22-0.40). During our study period, the estimated annual percentage change in incidence rates rose statistically significantly among men (6.04%/year, CI 2.02-10.21) and women (4.25%/year; CI 1.58-6.99). More cases were found in southern latitudes (< 38°, including San Francisco-Oakland, Hawaii, New Mexico, Atlanta, Los Angeles, San Jose-Monterey, and Rural Georgia) than in northern latitudes (> 40°, including Connecticut, Detroit, Iowa, Seattle (Puget Sound), Utah, and Alaska Native Tumor Registry), which contrasts with a prior U.S. study that demonstrated an increased incidence in northern latitudes. Overall survival and melanoma-specific survival was poor for men and women. The increasing incidence of anorectal melanoma and poor survival rates in both men and women warrant further investigation and confirmation in other populations. Furthermore, the observed greater incidence in women and in southern latitudes should be explored further in analytic studies.

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Prognostic factors in transformed mycosis fungoides: A retrospective analysis of 187 cases

R Talpur,¹ D Sui² and M Duvic¹ ¹ Dermatology, UT MD Anderson Cancer Center, Houston, TX and ² Biostatistics, UT MD Anderson Cancer Center, Houston, TX

Large cell transformation (LCT) (>25% tumor cells with nuclei > 4 times normal size) of mycosis fungoides (MF) is generally associated with aggressive clinical course and poor survival. In order to identify prognostic clinical, histologic and immunophenotype predictors of outcome associated with LCT, we performed a retrospective analysis of our cutaneous lymphoma database containing 1900 MF/Sézary syndrome (MF/SS) evaluated over 26 years. We identified 187 patients with biopsy proven LCT in skin or nodes for overall incidence of 9.8%: 168 had LCT in skin only, 19 had LCT in both skin and lymph nodes. Mean age was 59.57 years and male to female ratio was 1.2:1. As expected, LCT was uncommon among early patch/plaque MF (Stage IA-IIA) 17.1% patients and 83% of advanced Stage IIB-IVB patients. Progression to LCT within < 12 months after diagnosis occurred in 155 patients (82.89%) whose OS was 4.7 yrs and compared to 32 patients (17.11%) diagnosed with LCT within > 12 months after diagnosis whose OS was 7.13 (p=.08; NS). Death from disease occurred in 68 of 162 (42%) with cause of death available. There was no difference in survival in patients with LCT in skin or skin and nodes. Median overall survival of LCT patients (4.79 yrs) was similar to non-LCT (T3) MF patients (6.24 yrs) and significantly worse than all MF patients (26.26 years) (p=.001). OS for LCT patients > 60 years was 3.71 compared to 6.18 years in patients <60 yrs (p=.0001). Median OS of patients with LCT and advanced stage was 3.72 yrs vs 5.96 years for early stage MF (p=.0147). Sixty-seven of 187(35%) LCT patients had >10% expression of CD30 on tumor cells. In conclusion, by univariate analysis, risk factors associated with disease progression or death included advanced age, LCT diagnosis < 12 months of diagnosis, and presence of CD30 expression > 10%.

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Pigmentary phenotype and race are incomplete predictors of Fitzpatrick skin type

SY He,¹ WJ Boscardin,² CE McCulloch,² M Chren,¹ E Linos¹ and ST Arron¹ ¹ Dermatology, University of California, San Francisco, CA and ² Epidemiology & Biostatistics, University of California, San Francisco, San Francisco, CA

The Fitzpatrick skin phototype (FSPT) is a method to assess sunburn/tanning by evaluating patient-reported sensitivity to UV. Physicians often estimate FSPT based on race or appearance rather than asking the patient about burning or tanning. Physicians often assign ethnic minorities to FSPT IV-VI based on skin color; this method has proved unreliable. Given the increasing ethnic diversity in the US, we sought to clarify the assumption that FSPT can be visually estimated by determining whether race and pigmentary phenotype are predictive of FSPT in a racially diverse population. 3386 people completed a cross-sectional survey. Multivariate ordinal logistic regression was performed for FSPT on predictors of sex, age, hair, eye, and constitutive skin color, and race. Ten-fold cross-validation was performed and the mean absolute error and weighted kappa were calculated to evaluate accuracy. The entire range of FSPT I-VI was observed for all racial/ethnic groups. Hair, eye, and skin color were all independent predictors of FSPT; race was also an independent predictor even when controlling for pigmentary phenotype ($p < 0.01$). The predictive model had a weighted kappa statistic of 0.53 and mean absolute error of 0.916 for prediction within one level, suggesting that constitutive pigmentation and race are incomplete predictors of FSPT. While FSPT can be estimated by observation of pigmentation and race, these are incomplete predictors of tanning and burning ability. Race was also an independent predictor of FSPT, suggesting that genetic factors beyond pigmentation underlie response to UV radiation. All FSPT were observed in all racial groups. Given that the tendency to sunburn has been associated with skin cancer risk, accurate measurement of FSPT in ethnic minorities may predict skin cancer risk in these populations.

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Vitamin D intake and risk of incident psoriasis

JE Merola,¹ J Han,^{1,2} T Li² and A Qureshi^{1,2} ¹ Clinical Research Program, Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA and ² Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

The purpose was to examine the association between dietary as well as supplementary vitamin D intake and incident psoriasis in women. We conducted a cohort study of 70,436 US female nurses aged 48-74 enrolled in the Nurses' Health Study who did not have psoriasis at baseline in 1994 and who completed semi quantitative food frequency questionnaires in 1994, 1998, and 2002. The incidence of clinician-diagnosed psoriasis was ascertained and validated by self-reported questionnaires. 520 confirmed incident psoriasis cases were documented during 945,643 person-years of follow-up from 1994 June to 2008 June. Association between vitamin D intake and incident psoriasis was assessed using multivariable-adjusted cox regression analysis. After adjusting for age, smoking, body mass index, calorie intake and alcohol use, there was no significant association between total vitamin D intake (measured as dietary and supplementary vitamin D, combined) and the risk of psoriasis. Compared with women whose dietary vitamin D intake <100 IU/d, multivariate relative risks for psoriasis were 1.03 (95% CI, 0.77, 1.39) for 100-199 IU/d, 1.06 (95% CI, 0.78, 1.44) for 200-299 IU/d, 0.91 (95% CI, 0.62, 1.33) for 300-399 IU/d, and 1.07 (95% CI, 0.66, 1.74) for ≥400 IU/d ($P_{trend} = 0.84$). The multivariate relative risk for women who took supplementary vitamin D ≥400 IU/d was 1.05 (95% CI, 0.76, 1.43) compared with women who did not take supplementary vitamin D. In conclusion, our study does not support preventive roles of dietary or supplemental vitamin D intake for incident psoriasis.

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The Journal of Investigative Dermatology's experience in its first six months on Facebook

R Gamble,¹ B Gilchrist² and R Dellavalle^{1,3} ¹ Dermatology, University of Colorado, Aurora, CO, ² Dermatology, Boston University, Boston, MA and ³ Dermatology, Veterans Affairs Medical Center, Denver, CO

With the Journal of Investigative Dermatology (JID) having recently begun a Facebook page in July 2012, we reviewed post analytics and audience demographics to determine factors encouraging audience participation. The top 5 posts [date posted; users reached] with the largest reach were: Vitamin D, UVR and immunosuppression [12/3/12; 802], Autoantibody differences in DLE and SLE [12/4/12; 764], UV-induced wrinkle formation by induction of HSP70 expression in mice [11/30/12; 739], Immunity to sand fly saliva in rodents induces protection against leishmaniasis [12/3/12; 722], Gene profiling of narrowband UVB-Induced skin injury [11/20/12; 720]. The top 5 posts [date posted; users engaged] with most engaged users were: Sciton BroadBand Light treatments can change the expression of genes associated with the aging process [11/14/12; 498], Punctate palmpoplantar keratoderma is caused by mutations in the AAGAB gene [10/23/12; 225], The role of systematic reviews and meta-analysis in Dermatology [11/24/12; 209], The pathobiological mechanisms of psoriasis [9/19/12; 140], Atopic dermatitis treatment [11/26/12; 133]. The top 5 posts [date posted; users talking] with most readers talking about them were: Sciton BroadBand Light treatments can change the expression of genes associated with the aging process [11/14/12; 180], Atopic dermatitis treatment [11/26/12; 77], Punctate palmpoplantar keratoderma is caused by mutations in the AAGAB gene [10/23/12; 65], The pathobiological mechanisms of psoriasis [9/19/12; 55], The role of systematic reviews and meta-analysis in Dermatology [11/24/12; 48]. A diverse group accessed the Facebook page including users from 83 countries. The top three countries were India (25%), Brazil (22%), and the United States (10%). There was diversity among the popular posts, but the most popular posts tended to either have a more immediate clinical impact than the average post, or to relate to a prominent current topic in dermatology research (such as psoriasis and systematic reviews).

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SSc-overlap syndromes differ in disease progression from limited and diffuse SSc (on behalf of all DNSS centers)

P Moynzadeh, T Krieg and N Hunzelmann University of Cologne, Cologne, Germany

Systemic sclerosis (SSc) is a heterogeneous multisystem connective tissue disease, which originates as a consequence of an interaction between an altered immunologic process, vascular endothelial cell injury as well as an excessive production and accumulation of collagen and other ECMs, causing skin sclerosis and fibrosis of affected visceral organs. A very interesting subset includes patients with overlap syndromes, presenting with SSc features as well as symptoms of other rheumatic diseases. These represent a very remarkable selection of scleroderma patients, categorized either by the detection of specific antibodies, by specific clinical features and/or a certain genetic background. Among all registered 3365 patients, 10% were classified as an overlap syndrome, while 48% were diagnosed with limited SSc and 30% with diffuse SSc. Within the overlap cohort 15 % had anti-centromere antibodies (ACA) and 13% were anti-Scl-70 antibody positive, while the remaining patients harboured other antibody specificities (66%). Within this group of 216 patients with other antibodies, 32% were U1RNP positive, 16% showed PmScl antibodies (Ab), 24% Ro-, 11% La-, 5% anti-Mi2-, 4% Jo1-, 2% PL-7-Abs, and 13 % were positive for rheumatoid factor. Detailed analysis of different organ manifestations revealed, that 59% of overlap patients suffered from musculoskeletal involvement, followed by 52% with GI-manifestation, 35% with lung fibrosis, 12% with heart involvement, 11% with PAH and 7% with renal manifestation. The Kaplan-meier analysis revealed a clear inclined position of overlap patients between patients suffering from the limited and diffuse form of SSc, especially regarding lung fibrosis and heart involvement (log rank <0.0001). The clinical data indicate that patients suffering from overlap syndromes have to be viewed as a separate SSc subset with a different course of disease, different proportional distribution of organ manifestations and antibodies.

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Inverse relationship between melanoma death and sentinel lymph node metastases by age in the SEER Databases (2003-2009)

MW Cavanaugh-Hussey,¹ EW Mu,¹ T Wang,¹ CM Balch² and S Kang¹ ¹ Dermatology, Johns Hopkins Medical Institutions, Baltimore, MD and ² Surgical Oncology, University of Texas Southwestern Medical Center, Baltimore, MD

It is known that elderly melanoma patients have lower survival rates than younger patients with melanoma. Paradoxically, a few smaller institutional studies have found a lower frequency of sentinel lymph node positivity in the elderly. This is the first study to examine these relationships across all age groups in a large national sample. The US Surveillance Epidemiology and End Results (SEER) Databases were queried to examine 122,721 melanoma cases from 2003 to 2009. Controlling for tumor depth, prevalence rates of sentinel node involvement and melanoma death were assessed for all age groups. The associations between age, nodal status, and mortality were then estimated using logistic regression analyses, controlling for tumor depth, ulceration, primary tumor site, histological subtype, and lymph node surgery. At each tumor depth >1 mm, older patients had less frequent sentinel node involvement but higher melanoma mortality than younger patients ($P < .001$). This inverse relationship was linear across all age groups. In multivariate regression analyses, >80 year-olds were less likely to be node positive compared to 0-20 year-olds (OR 0.38, 95% CI 0.26-0.54). Yet, >80 year-olds were more likely to die of melanoma compared to 0-20 year olds (OR 6.60, 95% CI 3.44-12.69). Similarly, this inverse relationship was seen across all age groups in the multivariate analyses. In a large national sample, we found an inverse relationship between melanoma death and sentinel lymph node positivity by age. This paradox highlights the need for further study into age related differences in melanoma biology, immunological surveillance, and host response. It also questions whether melanoma staging should take into account the age of a patient.

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Sun exposure, tanning bed usage and prevalence of atopic dermatitis

L Lin,^{1,2,4} J Han,^{1,2,3} Z Zhang,⁴ CA Camargo^{2,3} and AA Qureshi^{1,2} ¹ Clinical Research Program, Department of Dermatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ² Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, ³ Department of Epidemiology, Harvard School of Public Health, Boston, MA and ⁴ School of Public Health, Guangxi Medical University, Nanning, China

We sought to investigate the associations between eczema (atopic dermatitis, short as AD) and outdoor sun exposure, tanning bed usage, and UV index of residence. We included a total of 66,750 participants from the large well-characterized Nurses' Health Study II cohort (NHSII) established in 1989. Lifetime prevalence of eczema was attained from the 2009 NHSII questionnaire. We used multivariate logistic regression models to estimate odds ratios (OR) to AD for sun exposure at high school/college and at age 25-35; tanning bed usage at high school/college and at age 25-35; and UV index at birth place, age 15, and age 30. We included 66,750 participants who completed the NHSII 2009 questionnaire and had answered questions on eczema, sun exposure and tanning bed usage. 6,764 AD cases were reported. We observe prevalence of AD decreased as outdoor sun exposure increased. Compared with the group with <1hr/wk of direct sun exposure in high school/college, the multivariable-adjusted OR of AD was 0.88 (95% CI: 0.80-0.98) for 2-4hr/wk, and 0.87 (95% CI: 0.79-0.96) for 5+hr/wk ($p_{trend} = 0.03$). The multivariable-adjusted OR of AD for direct sun exposure at age 25-35 was 0.85 (95% CI: 0.78-0.93) for 2-4hr/wk, and 0.82 (95% CI: 0.75-0.89) for 5+hr/wk ($p_{trend} < 0.001$). However, we did not find a significant association between tanning bed usage with AD prevalence in either high school/college or age 25-35. No significant association was found between UV index of residence and AD prevalence. In conclusion, direct outdoor sun exposure may be associated with lower AD prevalence.

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Comparison between treatments for adult and adolescent acne: Response to treatments and challenges to study

M Diakow,¹ S Rivas,¹ T Mammone,² W Lee¹ and AR Shalita¹ ¹ Dermatology, SUNY-Downstate Med Ctr, Brooklyn, NY and ² Basic Science Research, Estee Lauder Companies, Melville, NY

Acne vulgaris is a chronic inflammatory disease known to be a common condition in adolescents. However, an increasing number of patients over the age of 25 are being identified and referred for acne treatment. There has been limited data in the literature on acne in this adult cohort. We conducted a retrospective review of 5 clinical acne studies with a total of 94 patients. We found the prevalence of adult acne to be 26-45%. Acne in this cohort of adult patients differs from the acne seen in younger patients. Adult acne tends to be more common in women. Female adult acne patients comprised 68% of patients. In terms of lesion type, our adult acne patients had similar numbers of inflammatory and non-inflammatory lesions, 47% vs. 53%, respectively, whereas the adolescent acne patients had the values of 40% vs. 60%. Adult acne lesions are seen distributed predominately on the chin and jaw-line. Furthermore, the psychosocial impact of acne for adolescents is well documented. In adult patients the negative effects on quality of life need to be addressed through effective treatment options. Therefore, assessing the distinguishing features of acne in this adult cohort and assessing responsiveness to treatments remains a critical step towards developing treatments for adult patients. Across the five treatment modalities response to treatment was assessed objectively by calculating the percent change in inflammatory and non-inflammatory lesion counts from baseline. Across the five studies, adult acne patients showed substantial improvement. Topical retinoid use among adult acne patients showed significant reduction ($p < 0.05$) in lesion counts – 59% and 73%, respectively in inflammatory and non-inflammatory lesions. Blue-light therapy was also found to be effective for adult acne treatment, 43% and 50%, respectively in inflammatory and non-inflammatory lesions. Several factors including problems with sensitive and dry skin in this group might pose potential problems for study and treatment options.

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What are the most important questions to be answered in dystrophic epidermolysis bullosa (DEB) research? Results from the Spanish prioritization partnership

P Dávila-Seijo,¹ ÁNGELA Hernández-Martín,² E Morcillo-Makow,³ R De Lucas,⁴ E Domínguez,³ N Romero,⁵ E Monrrós,³ M Feito,⁴ L Carretero,³ B Aranegui,^{6,5} and I García-Doval^{6,1} ¹ Dermatology, Complejo Hospitalario de Pontevedra, Pontevedra, Spain, ² Dermatology, Hospital Niño Jesús, Madrid, Spain, ³ The Dystrophic Epidermolysis Bullosa Research Association (DEBRA) Spain, Marbella, Spain, ⁴ Dermatology, Hospital Universitario de la Paz, Madrid, Spain, ⁵ Dermatology, Clínica Universitaria de Navarra, Madrid, Spain and ⁶ Research Unit, Fundación AEDV, Academia Española de Dermatología y Venereología (AEDV), Madrid, Spain

DEB is a rare genetic disorder that causes blisters with minor trauma in skin and mucosa. Patients and health care professionals (HCPs) have to deal with numerous complications for which there are frequently no evidence-based therapies. Because the research budget is limited and the number of uncertainties is large, prioritizing the most important is mandatory. Priority Setting Partnership (PSP) methodology tries to ensure that those who fund health research are aware of what matters to both patients and clinicians. Objectives: To find and prioritize the most important uncertainties about treatment shared by DEB patients, carers and HCPs. Methods: A DEB PSP was done following the guidelines of the James Lind Alliance. Uncertainties were obtained from patients, carers and expert clinicians and they were prioritized in an explicit process. Results: In the consultation stage, 323 uncertainties were submitted by 58 participants. The duplicated and non-treatment uncertainties were removed and the remainder were reduced to a list of 24 most popular questions through an online voting process. They were prioritized in a final workshop where a final top 10 therapy uncertainties was selected. It includes interventions in wound care, itch and pain management, treatment and prevention of syndactyly, cancer and future therapies. Conclusions: The top 10 treatment uncertainties on the management of DEB provides guidance for researchers and funding bodies, in an effort to promote research in questions that are important to both clinicians and patients.

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Patient-assessed disease severity is a strong determinant of health-related quality of life in chronic hand eczema

C Apfelbacher,¹ E Weisshaar,² S Molin,³ A Bauer,^{4,7} V Mahler,⁵ U Mattered,² M Weiss,² J Schmitt,^{6,7} T Ruzicka,³ P Elsner⁸ and T Diepgen² ¹ Institute of Epidemiology and Preventive Medicine, University of Regensburg, Regensburg, Germany, ² Department of Clinical Social Medicine, University of Heidelberg, Heidelberg, Germany, ³ Department of Dermatology and Allergy, Ludwig-Maximilians-University Munich, Munich, Germany, ⁴ Department of Dermatology, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany, ⁵ Department of Dermatology, University of Erlangen, Erlangen, Germany, ⁶ Institute and Outpatient Clinics of Occupational and Social Medicine, Technical University Dresden, Dresden, Germany, ⁷ University Allergy Center, University Hospital Carl Gustav Carus, Technical University Dresden, Dresden, Germany and ⁸ Department of Dermatology and dermatological Allergy, Friedrich-Schiller-University Jena, Jena, Germany

The purpose of this study was to analyse determinants of health-related quality of life (HrQoL) in patients with chronic hand eczema (CHE), using data from the German carpe (German acronym: Chronisches Handekzem-Register zum Patienten-Langzeitmanagement) registry. HrQoL was measured by the Dermatology Life Quality Index (DLQI). Demographics, disease-related variables, treatment-related variables, predisposition, health care utilization and treatment experience were entered into a multivariable linear regression model. Median DLQI was 8.00 (N=992). Self-assessed disease severity emerged as the strongest significant determinant ($\beta=0.38$) in the final model (N=582), followed by having experienced unpleasant side effects ($\beta=0.16$), general treatment burden ($\beta=0.11$), physician global assessment ($\beta=0.11$), atopic skin diathesis (0.09) and having visited a GP (0.09). Age, gender, body mass index, itch, localisation and duration of CHE, satisfaction with care as well as type of treatment did not emerge as significant determinants in the final model. 39% of the variance were explained by the variables considered. To conclude, self-assessed disease severity is a powerful determinant of HrQoL in CHE. Unpleasant side effects require special attention in the care of patients with CHE.

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High prevalence rates of occupational hand eczema among dental workers in Japan

K Minamoto,¹ T Watanabe² and T Diepgen³ ¹ Department of Preventive and Environmental Medicine, Graduate School of Life Sciences, Kumamoto University, Kumamoto, Japan, ² Watanabe Dental Clinic, Kumamoto, Japan and ³ Department of Social Medicine, Occupational and environmental dermatology, University of Heidelberg, Heidelberg, Germany

Objectives: To estimate the prevalence rates of work related hand eczema and its risk factors in dental workers in Japan. Methods: Population based cross sectional study among workers in dental clinics in Kumamoto city, Japan. Self-reported questionnaire based on the validated Nordic Occupational Skin Questionnaire 2002, consisted of hand eczema history, allergic disease history, glove use, hand washing, and other risk factors. In addition, patch testing was performed with 25 dentistry-related allergens in a subsample. Results: Out of 309 dental clinics to which the questionnaires were sent 97 clinics responded with 529 workers in total (dentists 19.5%, dental hygienists 50.3%, dental technicians 4.2 %, assistants 14.7%, and receptionists 11.3%). The mean age was 37.3 years and 78.1% of the 529 dental workers were female. In total, 55.1% of those workers answered to have a life-time history of hand eczema. The one-year prevalence and point prevalence were 38.9% and 18.7%, respectively. The highest prevalence rates were found in dental hygienists, assistants, and receptionists. The most frequent risk factors for work related hand eczema were soap for hands, gloves, powder of gloves, disinfectants of hands, alcohol, detergents for tools. 51 workers were patch tested. 2 of those were diagnosed as allergic contact dermatitis to acrylates and 4 to rubber chemicals. Conclusions: The prevalence rates of work-related hand eczema in dental workers are high and measures of primary and secondary prevention have to be established in Japan.

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High prevalence rates of contact allergy in the European general population

TL Diepgen,¹ L Naldi,² M Bruze,³ S Cazzaniga,² P Coenraads,⁴ P Elsner,⁵ R Ofenloch¹ and A Svensson¹ ¹ Clinical Social Medicine, University Hospital Heidelberg, Heidelberg, Germany, ² Centro Studi GISED, Bergamo, Italy, ³ University Hospital Malmö, Malmö, Sweden, ⁴ Department of Dermatology, University Hospital Groningen, Groningen, Netherlands, ⁵ Department of Dermatology and Allergy, University Hospital Jena, Jena, Germany and ⁶ University Hospital Coimbra, Coimbra, Portugal

The objective was to obtain reliable estimates of the prevalence rates of skin diseases and contact allergy to common allergens in the general population. The methods include cross-sectional study of a random sample from the general population, aged 18 to 74 years, in 6 different European areas (Sweden, The Netherlands, East-Germany, West-Germany, Italy, Portugal). In total 12,377 subjects were interviewed and a random sample (n=3,119) patch tested to True test panel 1, 2 and 3. A positive patch test reaction (at least a "+" reaction) is considered as a proxy for contact allergy. The reported lifetime prevalence rates (age-standardized) of diagnoses confirmed by a physician were as follows: contact dermatitis n=1025 (8.4%; 95%CI 8.0-8.8), atopic dermatitis n=870 (7.0%; 95%CI 6.7-7.3), other types of eczema n=1642 (13.4%; 95%CI 12.9-13.6). In total, 18.9% of all patch test subjects had at least one positive reaction to an allergen of True test panel 1 (men 9.0%, women 27.0%), 8.8% against at least one allergen of panel 2, and 1.0% at least one allergen of panel 3. At least one reaction against an allergen of True test panel 1, 2, or 3 was seen in 25.3% (men 15.7%, women 33.2%). The highest age-standardized prevalence rates (<1%) were found for Nickel sulfate (14.6%; 95%CI 13.7-15.5), Thiomersal (5.1%; 95%CI 4.5-5.7), Cobalt chloride (2.2%; 95%CI 1.8-2.6), and p-tert-Butylfenolformaldehydesin (1.3%; 95%CI 1.0-1.6). In conclusion, contact allergy is frequent in the general population and needs a carefully interpretation of its clinical relevance.

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Black henna tattoos but not hair colorants are an important risk factor for contact allergy to p-phenylene diamine in the European general population

TL Diepgen,¹ L Naldi,² M Bruze,³ S Cazzaniga,² P Coenraads,⁴ P Elsner,⁵ M Goncalo,⁶ R Ofenloch¹ and A Svensson³ ¹ Department for Clinical Social Medicine, University Hospital Heidelberg, Heidelberg, Germany, ² Centro Studi GISED, Bergamo, Italy, ³ University Hospital Malmö, Malmö, Sweden, ⁴ Dept. of Dermatology, University Hospital Groningen, Groningen, Netherlands, ⁵ University Hospital Jena, Jena, Germany and ⁶ University Hospital Coimbra, Coimbra, Portugal

Objectives: To assess the prevalence rate of contact allergy to p-phenylene diamine (PPD) and its risk factors in the general population in different European countries. Methods: In a cross-sectional study a random sample of the general population, aged 18 to 74 years, was investigated in 6 European areas (Sweden, The Netherlands, East-Germany, West-Germany, Italy, Portugal), 10,425 subjects were interviewed and a random sample (n=2,739) patch tested to PPD. Results: In total, 5286 (50.9%) reported to have used hair colorants at least once in their lifetime (females 78%, males 20%) and 35% used hair colorants during the last 12 months. Hair colorants avoidance because of any skin problem during lifetime was reported by 624 subjects (6%). 570 subjects (5.5%) had used black henna tattoos in lifetime. The overall age-standardized prevalence rate of PPD contact allergy was 0.8% (95%CI 0.6-1.0%) in both men and women, and hair colorant lifetime users and non users with no statistically significant differences. However the prevalence in black henna tattoo users was 3.2% vs. 0.6% in non-users ($p < 0.001$). A clinically relevant positive patch test reaction to PPD related to hair colorants (defined as lifetime avoidance of hair colorants and itchy skin rash on the scalp/face/ears during lifetime) was found in 0.1% (95%CI 0.0-0.2%). A strongly significant association with PPD positivity was observed for subjects who had black henna tattoos in their lifetime, with an age and gender adjusted OR of 9.33 (95%CI 3.45-25.26, $p < 0.001$). Conclusions: Black henna tattoos are an important risk factor for PPD contact allergy in Europe.

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The impact of localisation on the association of itch and acne. Results from a population survey among adolescentsF Dalgard and J Halvorsen *University of Oslo, Oslo, Norway*

Two small studies have shown an association between adolescent acne and itch. However, there is a need for population studies to better examine this relationship, especially regarding the localisation of lesions. The objective of this study was to examine the association between localisation of acne and itch in a large sample of adolescents from the general population in Norway. The design was a cross-sectional population-based study. All 18 or 19 year olds in their final year of schooling living in Oslo were invited to participate in our questionnaire. In total, 4744 adolescents were invited and 3775 (80%) completed the questionnaire. Study participants were asked to rate current severity of acne and itch intensity. The prevalence of itch among adolescents with facial acne was 17.6% (72/409), and the prevalence of itch among adolescents with acne on other body sites was 16.0% (12/75). In an adjusted logistical regression analysis controlled for mental distress, sex, family income and ethnicity, the adjusted odds ratio for acne and current itch was 2.43 (1.70-3.46) for those with facial lesions compared to 2.21 (1.05-4.64) among those with lesions on other body parts. The conclusion is that there is a higher and significant association between acne and itch among adolescents with facial lesions. This should be kept in mind in the management of adolescents with facial acne.

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Latent Cclass analysis of 697 patients with non-segmental vitiligo identify of two clinical subtypesK Ezzedine,¹ A le Thuaut,² T Jouary,¹ J Seneschal,¹ A Taieb¹ and S Bastuji-Garin² *1 Dermatology, Hôpital St-André, Bordeaux, France and 2 Public Health and Statistics, (1) Université Paris Est Créteil, LIC EA 4393 ; AP-HP, Hôpital Henri-Mondor, Créteil, France*

Non-segmental vitiligo (NSV) is a disease with variable clinical course. Our objective was to identify underlying subtypes of NSV that best explain the diversity NSV. We prospectively collected data of 697 consecutive new cases of NSV between 2007 and 2012. Latent class (LC) analysis was used to identify homogeneous groups of patients with similar clinical patterns. Demographic characteristics, localisation of lesions, disease activity and triggering factors were compared across LC. Median patient age was 33 years ; median age at onset was 19 years (range, 0.25-74). A two-class model showed the best fit (minimization of Bayesian Information Criteria). The LC1 patients (63% of the sample) had a high probability of late onset of the disease (0.93), and a lower probability of associated halo nevi (0.16), Koebner phenomenon (0.40), family history of vitiligo (0.25) and canities (0.24). The LC2 patients (37%) had high probabilities of very early onset of the disease before the age of 12 (0.92), associated halo nevi (0.40), Koebner phenomenon (0.47), lower surface involvement (< 3% of the body surface, 0.66); and family history of vitiligo (0.40). Logistic regression comparing LC1 and LC2 patients showed that involvement of the head was linked to LC1 (85.5% vs 75.4% for LC2) ($p<0.001$) whereas trunk and limbs localizations were more often seen in LC2 (respectively 69.8%; 81.9%) than in LC1 (respectively 59.0%; 65.3%). In addition, combination with atopic dermatitis or with another autoimmune disease was linked to LC2 as it was the case for familial background of autoimmune thyroiditis and other autoimmune disease. LC analysis allows identifying 2 distinct subtypes of NSV. This classification is in agreement with the current knowledge of vitiligo and may help to improve our understanding of autoimmunity/inflammation with respect to predisposing genetic factors already identified.

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Reliability study of four objective outcome measures for atopic dermatitisAQ Tran,^{1,3} JP Lazo-Dizon,^{1,3} J Kim,^{1,3} BS Daniel,^{1,3} SS Venugopal,^{1,3} LM Rhodes,^{1,3} MG Laws² and DF Murrell^{1,3} *1 Department of Dermatology, St George Hospital, Sydney, NSW, Australia, 2 Kirby Institute, Sydney, NSW, Australia and 3 University of New South Wales, Sydney, NSW, Australia*

It is not known which objective disease extent measure for atopic dermatitis is the most reliable. This study compared the inter-rater and intra-rater reliability of the four most commonly used outcome measures for atopic dermatitis: the objective SCORing Atopic Dermatitis (SCORAD), Eczema Area and Severity Index (EASI), Six Area, Six Sign Atopic Dermatitis (SASSAD) and Three Item Severity index (TIS), as well as analysing their correlation to three QOL instruments: the Patient-Oriented Eczema Measurement, Child/Dermatology Life Quality Index and SkinDex-29. After power calculations to determine the minimum number required, 12 atopic dermatitis patients having different degrees of severity were assessed on the same day by 5 independent trained dermatology assessors. Reliability was measured using the intra-class correlation coefficient calculated through one-way random effect ANOVA and Bland-Altman plots. Correlation between subjective and objective outcome measures was computed using the two-tailed Spearman's rho correlation with scatterplots. EASI demonstrated a high intra-rater and moderate inter-rater reliability, ICC=0.886 (95% CI: 0.744-0.952) and ICC=0.73 (95% CI=0.5 – 0.9), respectively. SASSAD showed moderate intra-rater and inter-rater reliabilities, ICC=0.720 (95% CI = 0.424-0.878) and ICC=0.68 (95% CI=0.44-0.88). TIS showed high intra-rater reliability ICC=0.886 (95% CI: 0.744-0.952) but low inter-rater reliability ICC=0.497 (95% CI=0.233-0.785). Objective SCORAD showed low intra-rater and inter-rater reliability, with ICC of 0.446 (95%CI=0.037-0.730) and 0.498 (95% CI=0.234-0.785), respectively. Only SASSAD demonstrated moderate correlation with SkinDex-29 $p=0.611$ ($p=0.035$). In conclusion, this study found that the EASI score was the most reliable objective outcome measure and supports the use of EASI as a routine extent measure for atopic dermatitis studies and possibly for routine clinical use.

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International validation of a quality of life instrument specific to cosmetics and physical appearance: The BeautyQoLA Beresniak,¹ GG Krueger,² S Talarico,³ K Tsutani,⁴ G Duru,⁵ J Auray,⁵ S Aractingi⁶ and Y de Linares⁷ *1 Research, Data Mining Int., Geneva, Switzerland, 2 Dermatology, Univ. of Utah, SL, UT, 3 Dermatology, Univ. of Sao Paulo, Sao Paulo, Brazil, 4 Public Health, Univ. of Tokyo, Tokyo, Japan, 5 Research, Cyklad, Lyon, France, 6 Dermatology, Paris-Descartes Univ., Paris, France and 7 Research Innovation, L'Oreal, Paris, France*

Objective: The BeautyQoL instrument is a multi-dimensional self administered questionnaire which has been specifically developed over three years in 16 languages for assessing the impacts of cosmetic products and physical appearance on Quality of Life (QoL). This study reports the main features of the validation process. Methods: An acceptability study was carried out on 874 subjects in France, UK, Germany, Spain, Sweden, Italy, Russia, USA, Brazil, Japan, India (Hindi and English languages) China and South Africa (Zulu, Sotho and English languages). 3231 subjects were then further recruited for completing i) the BeautyQoL questionnaire ii) key clinical skin attributes iii) the SF-36 generic QoL questionnaire and iv) a socio-demographic questionnaire. Psychometric properties, construct validity, reproducibility, internal and external consistency were evaluated. Results: Acceptability was high among the 16 cultures. The validation process condensed the questionnaire into 42 questions structured in five dimensions, explaining 76.7% of the total variance: Social Life, Self confidence, Psychological life, Energy and Attractiveness. Internal consistency was high (Cronbach alpha coefficients between 0.932 and 0.978). Reproducibility at 8 days was satisfactory in all dimensions. An algorithmic scoring procedure allows calculating an overall score (index) and five sub-scores for each dimensions (profile). External validity testing revealed that the five BeautyQoL scores correlated significantly with all SF-36 scores, Physical Function excepted. Conclusions: Results demonstrate both the validity and reliability of the BeautyQoL questionnaire as the very first international instrument specifically dedicated to cosmetic products and physical appearance.

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Incidence and mortality of bullous pemphigoid in Olmsted County, Minnesota, USA over five decadesC Weaver, C Lohse, M Pittelkow, M Camilleri, M Al-Hashimi, A Weaver and C Wieland *Dermatology, Mayo Clinic, Rochester, MN*

Bullous pemphigoid (BP) is a chronic autoimmune blistering disease that occurs predominantly in the geriatric population. Studies from Europe have shown an increased incidence of BP, and there is evidence to suggest BP is associated with an increased mortality rate. The Rochester Epidemiology Project was used to identify 101 patients who were residents of Olmsted County, Minnesota at their first lifetime diagnosis of bullous pemphigoid (BP) between January 1, 1950 and December 31, 2009. Incidence rates per 100,000 person-years were calculated using incident cases of BP as the numerator and age- and sex-specific estimates of the population of Olmsted County, Minnesota as the denominator. The age- and sex-adjusted incidence of BP was 2.6 per 100,000 person-years (95% confidence interval [CI] 2.1-3.1). Age-adjusted incidence was 2.5 per 100,000 person-years (95% CI 1.9-3.1) for females compared to 2.7 per 100,000 person-years (95% CI 1.8-3.5) for males ($p=0.65$). Incidence of BP increased significantly with age at diagnosis ($p<0.001$) and over time ($p<0.001$). Overall survival was estimated using the Kaplan-Meier method. Estimated overall survival rates (95% CI; number still at risk) at 2, 4, 6, 8, and 10 years following diagnosis were 71% (62 – 80; 64), 53% (43 – 64; 47), 39% (30 – 50; 31), 31% (23 – 43; 23), and 26% (18 – 38; 15), respectively. In comparison, the survival rates at these time points expected in the Minnesota white population were 85%, 72%, 61%, 51%, and 42%, respectively. The survival observed in the incident BP cohort was significantly poorer than expected ($p<0.001$). Patients with bullous pemphigoid had a standardized mortality ratio of 1.82 (95% CI 1.42 – 2.28). These results from the United States support previous reports of increased, though less marked mortality of BP compared to that reported in Europe.

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Inpatient pseudocellulitis: Assessing the extent of the problem through dermatology consultation servicesL Strazula,¹ J Cotliar,² LP Fox,⁴ S Gee,³ SL Hughey,⁵ K Shinkai⁴ and D Kroshinsky¹ *1 Massachusetts General Hospital, Boston, MA, 2 Northwestern Medical Center, Chicago, IL, 3 University of California Los Angeles Medical Center, Los Angeles, CA, 4 University of California San Francisco Medical Center, San Francisco, CA and 5 University of Alabama, Tuscaloosa, AL*

Due to the many dermatological conditions that can mimic cellulitis, pseudocellulitis is commonly encountered by inpatient dermatology consultation teams. In order to better quantify and qualify the nature of this problem, we conducted a retrospective review of inpatient dermatology consultations in 2008 across four academic medical centers to assess the number of consultations requested for cellulitis, the incidence of pseudocellulitis, and risk factors associated with the diagnosis. In 2008, a total of 1,430 inpatient dermatology consultations were conducted at Massachusetts General Hospital, University of California Los Angeles Medical Center, University of Alabama Medical Center, and University of California San Francisco Medical Center. Of these, 75 (5.24%) were requested for the evaluation of cellulitis. There were 34 women and 36 men with a mean age of 56.5 years. 65 (86.67%) of these patients were admitted to the hospital for the evaluation and treatment of their rash. After evaluation by dermatology, 20 (26.67%) patients were found to truly have cellulitis whereas 55 (73.33%) patients were diagnosed with pseudocellulitis. The most common mimicking diagnoses were stasis dermatitis (28%), contact dermatitis (12%), and tinea pedis (10.67%). The most common risk factors found in all patient evaluated for cellulitis were a history of skin disease (24%), diabetes mellitus (19%) and active cancer (17.33%). The misdiagnosis of cellulitis is a significant problem among hospitalized patients. Early dermatology consultation in order to establish a correct diagnosis may decrease unnecessary antibiotic usage and shorten hospital stays. Obtaining a dermatology consultation in the outpatient or emergency room setting may be a cost-effective strategy to decrease overall hospital admission rates.

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Life-style factors associated with hidradenitis suppurativa

VI Reeder,¹ DA Gold,¹ M Mahan,² IH Hamzavi¹ and HW Lim¹ *1 Department of Dermatology, Henry Ford Medical Center, Detroit, MI and 2 Department of Public Health Services, Henry Ford Medical Center, Detroit, MI*

Hidradenitis suppurativa (HS) is a chronic inflammatory disease of the skin that is incompletely understood. Knowledge of disease associations may further the comprehension and management of this condition. Our aim was to create a formal database of information gathered from individuals with the diagnosis of HS seen in a specialty dermatology clinic. First, a standard, self-reported questionnaire on life-style factors was administered to 88 patients. Subsequently, a retrospective chart review from January 1, 2011 to May 31, 2012 was performed. Charts of patients with the ICD 9 code for HS were evaluated. 366 subjects who met clinical criteria for HS were included in the database. A control population for the database was created from subjects seen in the same clinic during the same time period for the diagnoses of keloids or verruca vulgaris using the matching criteria of age \pm 5 years, race and gender. Based on the self-reported questionnaire results, 69.9% of HS patients were obese, 49% of HS patients admitted to consuming fast-food two or more times per week, and 56.3% of HS patients reported no leisure-time physical activity. Subsequent review of the HS database revealed that in patients with the appropriate data available, 74.7% (204 of 273) HS subjects were found to be obese while only 25.3% (69 of 320) of the controls met this criterion. This was statistically significant ($p < 0.001$) and the odds ratio was 3.52 (2.48, 5.00). 43.8% (98 of 224) of HS patients and 22.5% (56 of 249) of controls were noted to have hypertriglyceridemia. This was statistically significant ($p < 0.001$) and the odds ratio was 1.54 (1.07, 2.22). 54.4% (199) of subjects were black and 25.7% (94) of subjects were white. The average age was 39.2 years. There is a significant relationship between lifestyle factors and this disease, which should further be investigated to evaluate a possible metabolic pathway for HS.

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Clinical factors and outcomes associated with invasive melanoma biopsy transection

JL Woodcock,¹ A Bowen,¹ Y Zhang,² G Stoddard² and K Callis Duffin¹ *1 Dermatology, University of Utah, Salt Lake City, UT and 2 School of Medicine, University of Utah, Salt Lake City, UT*

A recent audit of dermatopathology reports from the University of Utah Department of Dermatology revealed that 31% of invasive melanomas biopsies were deeply transected. To gain further insight, chart review of 85 invasive melanoma cases biopsied by departmental providers from 6/1/10 to 5/10/11 was conducted. A mixed effect model was used to adjust for cluster effects within providers. Some of the clinical factors included in this model were the dermatopathologist evaluating the specimen, patient age, sex, and past medical history; family history of melanoma, whether the clinician expressed concern regarding melanoma on the pathology requisition, biopsy site, and type of biopsy. Histologic characteristics included in the model were Breslow depth, Clark level, type of melanoma, and presence of lateral transection. Some of the outcome variables that were assessed included excision margins, whether residual melanoma was present on re-excision, whether sentinel node biopsy was performed, and whether the sentinel node biopsy was positive. This study revealed that all deep transections occurred with shave biopsies ($p = 0.05$). Other clinical factors that were statistically associated with transection included lack of clinical suspicion for melanoma ($p = 0.02$), female patient ($p = 0.03$), and non-trunk location ($p = 0.05$). Patients with deeply transected melanomas were more likely to get sentinel node biopsies (71% vs. 30%, $p = 0.001$). Given that all transected melanomas were biopsied via shave technique, questions arise as to why this technique was chosen by clinicians. Decreased diagnostic accuracy is a possibility given that a lack of clinical suspicion was significantly associated with biopsy transection. Concern regarding cosmesis or the time constraints of an excisional biopsy may cause clinicians to compromise optimal clinical practice. Further studies are needed to elucidate these factors, but the increased rate of sentinel node biopsies in transected melanomas makes this an important clinical question.

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Fragrance contact allergy in the European general population

TL Diepgen,¹ L Naldi,² M Bruze,³ S Cazzaniga,² P Coenraads,⁴ P Elsner,⁵ M Goncalo,⁶ R Ofenloch¹ and A Svensson¹ *1 Department for Clinical Social Medicine, University Hospital Heidelberg, Heidelberg, Germany, 2 Centro Studi GISED, Bergamo, Italy, 3 University Hospital Malmö, Malmö, Sweden, 4 University Hospital Groningen, Groningen, Netherlands, 5 University Hospital Jena, Jena, Germany and 6 University Hospital Coimbra, Coimbra, Portugal*

Objectives: To determine the prevalence of fragrance contact allergy in the European general population and to assess the clinical relevance of positive patch test reactions to different fragrances. **Methods:** Cross-sectional study in a random sample of the general population, aged 18 to 74 years, in 6 European areas (Sweden, The Netherlands, East-Germany, West-Germany, Italy, Portugal), 12,377 subjects were interviewed about lifetime, 1-year and point prevalence of any skin disease and history of exposure to products containing fragrances, metals, plastics, rubber, leather, hair dye, with frequency and pattern of use. A random sample ($n=3,119$) patch tested to the European standard series True test panel 1, 2, 3 and 20 fragrances in Finn Chambers. **Results:** The conservative prevalence of fragrance contact allergy (defined by the existence of a positive patch test to Fragrance Mix I (FM I) or Fragrance Mix II (FM II) or any of the individual materials in either FM I or FM II or Peru Balsam or sesquiterpene lactones or 3 and 4-(4-Hydroxy-4-methylpentyl)-3-cyclohexene-1-carboxaldehyde (HMPCC) that show clinical relevance defined conservatively as lifetime avoidance of scented products and contact dermatitis in a lifetime or an itchy skin rash lasting more than 3 days in a lifetime, respectively is 0.8% and 1.9%, respectively. This compares to a prevalence of up to 14% reported in clinics in dermatitis patients. The prevalence rates of contact allergy to fragrances in females are about two times higher than in males in very country. **Conclusions:** There was a substantially lower prevalence rate of fragrance contact allergy in the general population in Europe as compared to previously published clinical data.

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Recurrent cellulitis in outpatient primary care: assessing the nature of the problem

L Strazzula and D Kroshinsky *Massachusetts General Hospital, Boston, MA*

Cellulitis is a significant problem in outpatient medicine and recurrent disease represents a growing challenge. In efforts to better quantify and qualify the population affected by recurrent cellulitis, we conducted a retrospective chart review from 2008-2011 of adult patients diagnosed with cellulitis at least twice in a given year at five outpatient primary care clinics or the Emergency Department (ED) at Massachusetts General Hospital. Patients who presented to the ED and were subsequently admitted were excluded. Over 1,000 medical records were reviewed yielding 140 patients meeting criteria for recurrent cellulitis and representing a total of 342 outpatient diagnoses. There were 59 (42.1%) women and 81 (57.9%) men with a mean age of 61.0 years. Patients had a mean of 2.3 diagnoses per year with as many as five diagnoses observed in three patients. 100% of patients received oral or intravenous antibiotics for each cellulitis diagnosis. The most common risk factors associated with recurrent cellulitis diagnosis were a history of inflammatory skin disease (42.9%), chronic lymphedema (35.0%), a history of trauma (35.0%), and diabetes (22.9%). An objective marker of infection such as fever >100.5 F was only present in 1.9% of cases, whereas leukocytosis was present in 19.5% of diagnoses. 17 patients (12.1%) had significant adverse events related to antibiotic usage such as drug rash, drug-induced vasculitis, and Clostridium difficile infection. Cellulitis is a considerable problem in medicine, with many patients having multiple bouts in the outpatient primary care setting alone. This study attempts to quantify the nature of the problem at one large medical center to guide future studies. Given the high prevalence of chronic skin disease and lymphedema in this population, we believe that a substantial proportion of these patients may have had pseudocellulitis rather than a true infection. A collaborative effort between primary care physicians and dermatologists may help identify potential mimicking conditions and modify contributing risk factors to reduce the burden of disease.

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Pilot study of skin aging peculiarities in patients with metabolic syndrome

J Janovska,¹ J Voicehovska,² J Kisil,¹ R Kleina³ and R Karls¹ *1 Dermatology, Riga Stradinsh University, Riga, Latvia, 2 Internal Disease, Riga Stradinsh University, Riga, Latvia and 3 Pathology, Riga Stradinsh University, Riga, Latvia*

Introduction: Overweight and obesity in youth is a worldwide public health problem. Worldwide approximately 15% of population has got a metabolic syndromes (M. Hanefeld 2010) aged 40-75 years old. Metabolic syndrome involves damage to various organs via oxidative stress or inflammation, similar to the changes associated with aging. **Aim:** The aim of our pilot research is to compare skin histological condition in patients with metabolic syndrome (MS) and without it. **Material and methods:** Generally we have evaluated 13 patients, 7 of them had MS. The research was divided into several steps: clinical examination, blood tests and punch biopsy. Punch biopsy 3-4 mm deep was taken from the dorsal surface of the palm. Specimens were stained with haematoxylin-eosin and with Trichrom Masson, immunohistochemically CD 34, CD 117, CD20, CD8 and bcl-2 were detected. Capillaries, CD 117, CD3, CD20, CD8 cells and fibers were calculated per 1 mm² but adipocytes, were measured by magnification 40x with ruler of Axiostar plus microscope. Bcl-2 expression was evaluated per 100 cells. All data was analyzed by SPSS 17.0, Excel programs. **Results:** Women: Men ratio was 1, 6: 1. Mean age for both genders was 48.1 years old. In group of MetSy common histological pattern were: hyperkeratosis, granulosis, dermal fibrosis and a subtle infiltrate around blood vessel composed of T lymphocytes. Acanthosis, or thickening of the stratum spinosum, is typically mild in patients with MetSy. Immunoreactivity for bcl-2 protein has patchy pattern in basal cells with average amount of 39, 1 per 100 basal cells in MetSy and 6, 4 in persons without it. **Conclusions:** Decreased epidermal vascularization, because of thickness of blood vessels in dermis may lead to premature skin aging manifestations or at least may impact the proliferation of keratinocytes. The mononuclear infiltration around blood vessels shows us the inflammatory component of metabolic syndrome which can be caused by oxidative stress.